# SCIENCE

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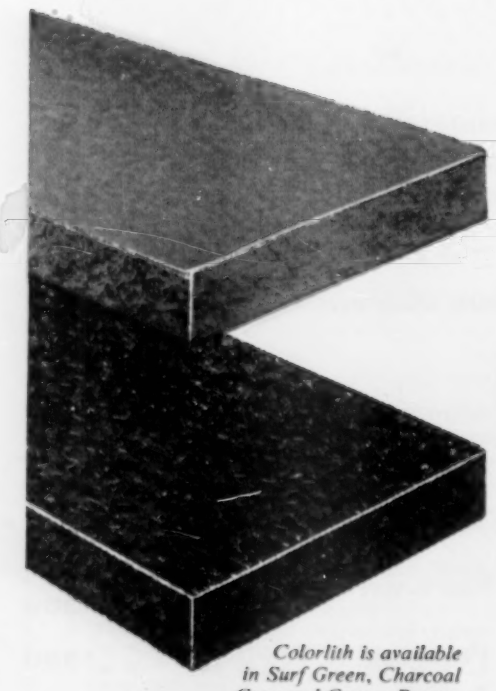

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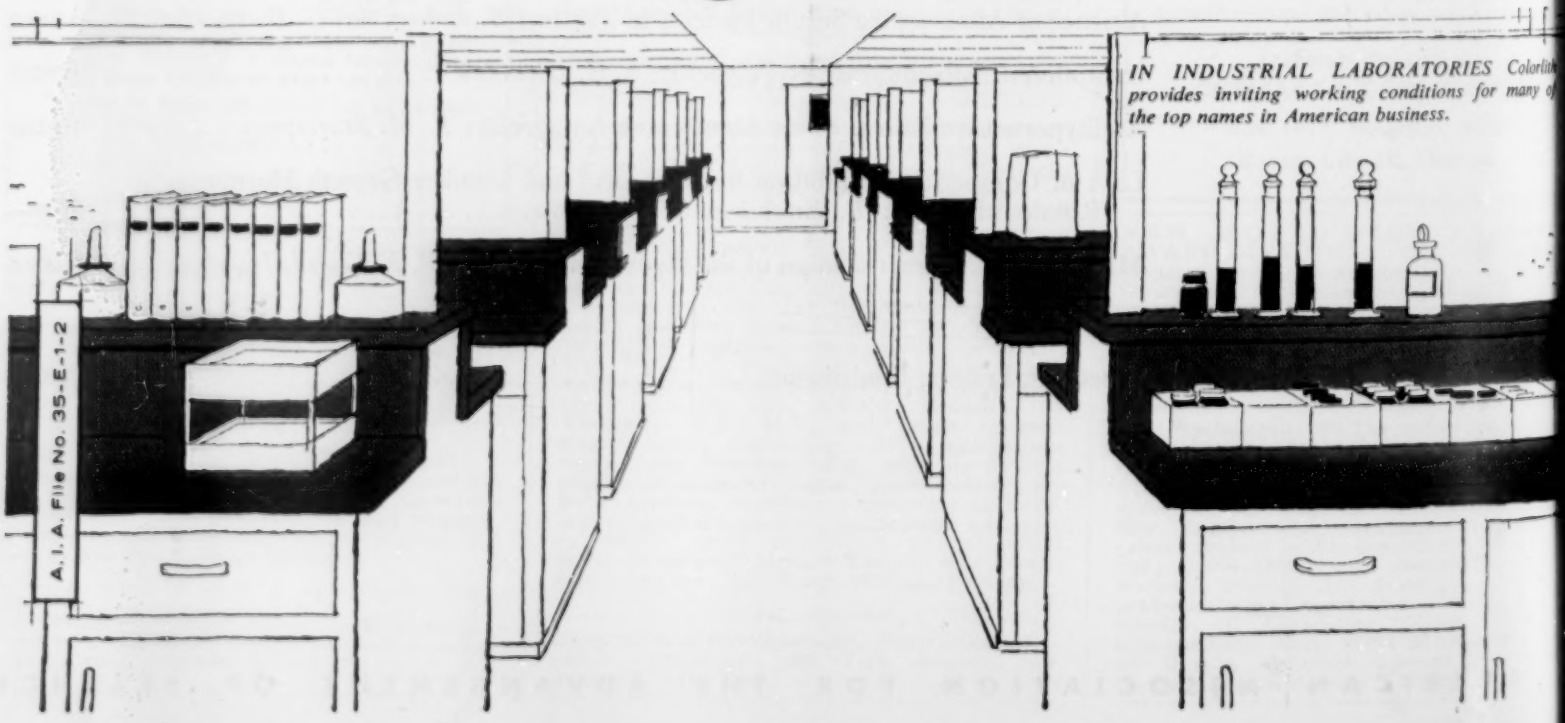


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## Space Is Money

Among the problems facing the present effort to set up a government agency to direct a civilian space program is the familiar one of establishing appropriate pay provisions. The administration bill, which was submitted by President Eisenhower on 2 April, and the House bill, which was approved on 1 June—the House taking less time than the Senate to reach this stage in the legislative process—agree on the point that the 43-year old National Advisory Committee for Aeronautics should serve as the nucleus for a National Aeronautics and Space Administration. The two bills disagree, however, about the provisions that should be included in the space act to enable the new agency to recruit and hold scientists of the desired talent.

A problem of enlisting scientists in certain fields for government research arises because the salary levels allowed by civil-service classifications are not always competitive with those that private companies are prepared to pay. In the past one solution, for certain agencies, has been to provide by law a certain number of scientific positions at somewhat higher levels of pay. A second solution, which is less straightforward but which has produced considerably higher salary levels, has been to put scientific personnel on the payroll of private corporations expressly created to evade the civil-service limitations.

In facing the problem of salaries for the staff of the space agency, the administration bill takes an approach which could produce salaries considerably above those of the civil-service scale. It would exempt the agency from civil-service limitations, authorizing it, in the President's words, "to fix the compensation of its employees at rates reasonably competitive with those paid by other employers for comparable work." The House bill recognizes the need for some kind of differential in salary level favorable to the space agency, but on a more modest scale. It would authorize up to 250 scientific positions paying $19,000 a year, and up to 10 more positions paying $21,000. At the time the House bill was voted, the maximum pay for comparable scientific positions in other agencies was $19,000, with NACA, for example, limited to 30 positions.

Unfortunately, any provision that favors one scientific agency at the expense of another creates fresh difficulties—the greater the imbalance the greater the difficulties. One difficulty is that the Government, in employing scientists, is to a large extent competing with itself. Agencies compete both with other agencies and with private companies holding cost-plus contracts with the Government. The result may be a pay spiral, which is unfortunate for taxpayers if not for the scientists immediately involved. Another difficulty is the possible adverse effect on the morale of those scientists who are not so fortunate as to belong to the favored group.

However, in the short run these difficulties as they bear on the space agency do not carry much weight, and the short run in this case may be the overriding consideration. The problem of trying to keep an unsatisfactory pay system from getting more unsatisfactory may be of less importance than that of providing the new agency with a staff that can produce a vigorous and creative research program. In fact, things being what they are, the degree of favoritism incorporated in the final version of the space bill will be one measure of the importance that Congress attaches to the scientific investigation of outer space.—J.T.

# The place of the Particle Accelerator in Basic Research...

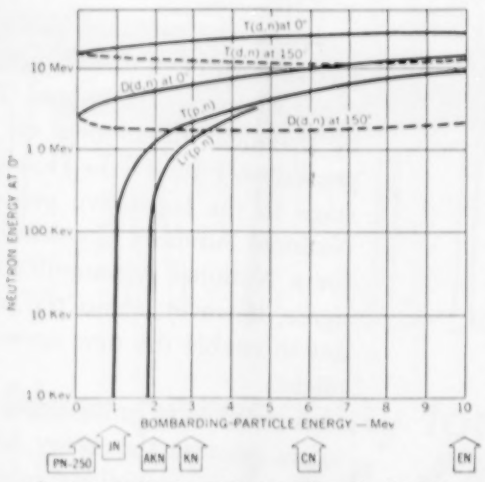
## Monoenergetic Neutrons—VII

Since their discovery in 1932, neutrons have been widely used in nuclear bombardment studies. Investigations of excited levels of compound nuclei produced by inelastic collisions with neutrons have enabled physicists to develop models describing these interactions.

### Accelerators Gave Control

The early work with neutrons was carried out with radioactive sources. The need for control and precision soon led to the use of particle accelerators as sources of monoenergetic neutrons. Studies were confined to the Mev range from exoergic reactions such as $H^2$ (d, n) $He^3$ and $H^3$ (d, n) $He^4$. Moderation of these fast neutrons was possible, but monoenergetic sources of slow neutrons could not be provided until the development of the atomic reactor in 1942. The subsequent use of monochromators made homogeneous beams of slow neutrons available.

Much work has been carried out with these thermal-neutron beams in measuring energy levels and spacings but, because of the dimensions of the crystal lattice, the maximum energy is confined to the order of tens of electron volts. The development of mechanical choppers has extended the energy range of monoergic neutrons to the low kev region, but even this method fails above about 20 kev.



Arrows indicate ratings of Van de Graaffs

### Fast Neutrons Needed

The only useful source of monoenergetic neutrons in the high kev range is provided by endoergic reactions of accelerated charged particles with suitable target nuclei. These reactions have threshold energies of the order of a few Mev. At this energy, the neutrons are emitted with the velocity of the compound neucleus. By varying the energy of the incident beam and the angle of observation, any neutron energy from about 30 kev to several Mev can be obtained. An excellent description of the angular-energy relationship has been given by Hanson, Taschek and Williams[1].

The most suitable reactions for monoenergetic-neutron production are $H^3$ (p, n) $He^3$ and $Li^7$ (p, n) $Be^7$. The former has a threshold of 1.019 Mev and the latter, 1.88 Mev. While the tritium reaction has a broader energy range than the $Li^7$ reaction, it is difficult to use. The gas must be adsorbed on a suitable metal and care taken to keep the temperature below 100°C. Gas targets have been used but require a thin window between the vacuum system and the gas chamber, producing energy spread in the proton beam. Lithium is a more suitable target material, but above neutron energies of about 600 kev a second neutron group appears.

### Variable Monoenergetic Beam Needed

The range of energies available depends on the energy of the incident proton beam, as shown above. The accelerator must have a continuously variable energy if a wide variation of neutron energy is to be obtained.

Neutron energy homogeniety is limited by target thickness, scattering material near the neutron target, and finally, the energy homogeniety of the proton beam. The former are experimental variables. The latter is an inherent property of the accelerator. Monoenergetic beams from the Van de Graaff® have long been considered to be the most suitable for this type of work, and leading nuclear physics laboratories throughout the world are now using Van de Graaffs built by High Voltage Engineering Corporation.

References.
1. A. D. Hansen, R. F. Taschek, J. H. Williams, Revs. Mod. Phys. 21, 635, 1949.

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## Procollagens

A citrate-soluble fraction of collagen is assumed to form a special group of connective tissue proteins.

V. N. Orekhovitch and V. O. Shpikiter

Connective tissue proteins are attracting a lot of attention, and many works have been devoted to them. If we consider only procollagen, with which we are going to deal in this article, this protein alone has already been the subject of a great number of researches. The relevant communications are so numerous that, frankly speaking, we are in a predicament, finding it entirely impossible to discuss them more or less comprehensively in this report. So far, we are not in a position to make any generalizations on the basis of published works. The point is that many investigations on procollagen are in the stage of experimental development as yet, and therefore a generalization of theoretical and practical significance may be expected only in the future. To cope with this situation, we have decided to report only the results of some investigations on procollagen carried out in our laboratory and published in Soviet and foreign scientific literature.

In our researches on proteins of the skin, we found in the latter a protein fraction soluble in an acid citrate buffer solution. It appeared that the protein making up this fraction contains about 25 percent of glycine as well as about 25 percent of proline and hydroxyproline, its content of aromatic and sulfur-containing amino acids being low. These data pointed to the proximity of this protein to collagen, and, consequently, it should be considered one of the group of collagen-like proteins. We are accustomed to think that collagen, constituting the bulk of collagen fibers, is an insoluble protein. Therefore we assumed that the citrate-soluble fraction is the biological precursor of collagen, and we named it procollagen, implying thus that the soluble collagen serves to form the principal insoluble mass of collagen fibers.

A number of observations concerning the quantitative content of these proteins in various physiological and pathological states of the organism testified in favor of the conception that procollagen is the biological precursor of collagen. For instance, it is well known that, with aging of the organism, the rate of collagen accumulation in the tissues gradually decreases. It turned out that procollagen content sharply decreases with the aging of animals. In guinea pigs 10 days to 6 months old, procollagen content varies from 7 to 10 percent, whereas in aged animals (more than 8 months old) it decreases to 1 percent. Further, collagen accumulation and the formation of new collagen fibers is greatly inhibited in scurvy-affected animals. It appeared that in these animals procollagen content decreases sharply, twice as much as in the control animals. These results can be explained by the reduction in procollagen formation with aging and in scurvy; in these conditions the source of formation of new collagen fibers is exhausted. It goes without saying that these data cannot be regarded as direct proof; nevertheless, they raise our supposition about procollagen being the biological precursor of collagen to the status of probability.

The amino acid content of soluble procollagen and that of collagen insoluble under ordinary conditions have been studied repeatedly. In our respective researches, when comparing data on the amino acid content of procollagen with those quoted with regard to collagen in the well-known paper by Bowes and Kenten (*1*), we have noted a difference in the content of such amino acids as phenylalanine, histidine, proline, and hydroxyproline. The difference in the chemical composition of soluble and insoluble collagens was also discovered by a number of other investigators—for example, by Bowes, Elliot, and Moss (*2*). It might be assumed that in the process of transformation of procollagen into collagen there take place some, although small, changes in the chemical composition of the former, rendering it insoluble. We cannot, however, insist on such an assumption, since obtaining pure insoluble collagen involves certain difficulties, and one should always keep in mind the possibility of errors in interpreting such data.

It is worthy of mention that, as far back as in 1900, Zachariadés (*3*), after treating tendons of rat tails with acidified water, found a soluble collagen-like protein in the solution. In 1927–30 Nageotte (*4*) thoroughly investigated the phenomenon of the passing of tendon proteins into solution. He found various ways of isolating this protein from the solution, the protein precipitates being obtained in the form of fibers or gel. Nageotte affirmed that this protein, or collagen A, occurs only in the tendons of rat tails. Somewhat later Leplat (*5*) succeeded in proving that the above-mentioned protein, soluble in acidified water, may be found not only in the tendons but also in the skin of various animals.

Following Nageotte and Leplat, other researchers also began to study collagen A. Some of them arrived at the conclusion that collagen A and collagen are identical. It follows from our data, how-

The authors are affiliated with the Institute of Biological and Medical Chemistry of the Academy of Medical Sciences of the U.S.S.R., Moscow. Dr. Orekhovitch is a member of the Presidium of the Academy and director of the Institute. This article is based on a paper which Dr. Orekhovitch presented at Massachusetts General Hospital, Boston, in Dec. 1957, during a recent visit to the United States.

ever, that collagen A belongs to the procollagen group. It is true that some investigators entertain doubts about the expediency of applying the term *procollagen* to proteins which are very similar in chemical composition to collagen, and they prefer to call such proteins "soluble collagens." Others doubt whether proteins soluble in acid media are the precursors of collagens. The supposition is even expressed that the actual precursor of collagen is a fraction extracted with alkaline and neutral salt solutions. We shall revert to this matter later. Now we should like to note that the solution of these moot problems presents some difficulty. This is due to the fact that, so far, we are not in possession of sufficiently detailed data on insoluble collagen. Therefore it is difficult to tell how the transformation of soluble into insoluble protein (that is, of procollagen into collagen) takes place, whether it is accompanied by any chemical changes in procollagen, or whether only physical changes—a peculiar thickening of procollagen due to the formation of intermolecular bonds—are of significance. We prefer to use the term *procollagen* rather than *soluble collagen*. We believe that at present it would make no sense to enter into a discussion on terminology.

## Methods of Obtaining Procollagens

Now we shall dwell briefly on the methods of obtaining procollagens and their occurrence. The conventional method of obtaining procollagen is the extraction of minced tissue with a citrate buffer solution (*p*H 3.5 to 4). Each 24 hours the liquid is decanted, and a new batch of the buffer solution is added. This is repeated 3 to 5 times. Each extract is filtered twice through a paper filter. The protein is isolated from the filtrate, either by dialysis against tap water or a weak alkaline buffer solution or by precipitation by addition of acetone (up to 30 percent) or sodium chloride (up to 5 percent). Precipitates obtained by dialysis usually consist of needle-like formations resembling crystals. It should be mentioned that these are not true crystals from the crystallographic point of view, since x-ray investigation has shown no periodicity in the three spatial directions. The patterns obtained were similar to that of collagen. It is noteworthy that in dialyzing the filtrate against a limited volume of a phosphate buffer solution with *p*H of about 8, we succeeded in obtaining "crystals" up to 3 millimeters in length.

We have isolated procollagens from organs and tissues of man and from those of representatives of various classes of vertebrates. Procollagen content not only differs in various species of animals but also varies greatly in different tissues of the animals of the same species. Procollagen was isolated from the skin as well as from the stomach and bladder tissues of man. We failed to discover procollagen in the tissues of blood vessels and intestines. It was isolated from the skin of cattle, a rabbit, a dog, a cat, a pike perch, a chicken, a turtle, and a frog and from the tissues of dog stomachs, chicken goiters, and pike-perch swim bladders. Procollagen was found in small amounts in the skin of a grass snake. Small quantities of this protein are also contained in cattle tendons. We failed to isolate procollagen from the tissues of some invertebrates—namely, rainworms and pond snails; obviously there is no such protein in the tissues of these animals. It is necessary to emphasize that the conditions for extracting procollagen from the tissues of various animals are different. Thus, the most suitable materials for extracting procollagen from chicken skin are buffer solutions with *p*H 3.0 to 3.5, whereas solutions with *p*H 2.0 to 3.0 are the best for extracting protein from turtle skin.

## Incorporation of Labeled Compounds

A series of our investigations was devoted to the study of the incorporation of labeled compounds. These experiments were carried out with the aim of obtaining additional data in support of the assumption that procollagen is the biological precursor of collagen. With this object in view, we used glycine containing radioactive carbon in the carboxyl group. After a single injection of labeled amino acid, the animals were killed at different time intervals. Their skin was minced, and procollagen was extracted from it by treatment with a citrate buffer solution. It was shown by such investigations (the results of some of them are given in Table 1) that procollagen radioactivity during the first hours after the glycine injections rapidly increases and reaches a peak in 24 hours. Then it gradually decreases, and in 35 to 40 days its values approximate the values of collagen radioactivity which are characteristic for it during the initial period after the glycine injection. In contrast to procollagen, carbon-14 content of collagen exhibits a constant increase as a function of time after the radioactive glycine injection, and in 40 days its activity exceeds 7 to 10 times that of procollagen of the first extraction.

The characteristic change in the radioactivity of proteins obtained from the successive extractions of the skin, as a function of time, is of particular interest. Procollagens isolated from the first, the second, and the third extracts are characterized by a rapid incorporation of carbon-14 and its rather rapid elimination upon reaching the peak, whereas with proteins isolated from the subsequent extracts, such a regularity is somewhat disturbed. In this case one may observe either a certain decrease in the rate of carbon-14 elimination or an increase in the content of radioactive carbon with time, which, as noted above, is typical of collagen as well. Such a phenomenon permits us to consider procollagens of the successive extractions as transient forms of this protein, from the most metabolically active to the least active, and, ultimately, to collagen.

Indeed, if we take into consideration the fact that, by the time the greatest amounts of radioactive collagen have formed, the bulk of carbon-14 should have been eliminated from the organism and that consequently there is no sufficient source of radioactivity left, then this process of change in the radioactivities of procollagen and collagen can be pictured as follows. During the first 24 hours after the introduction of the tracer, procollagen is synthesized, chiefly at the expense of the carbon-14 of the glycine. Therefore, the protein obtained in the first extraction is very rich in radiocarbon. Protein fractions passing into solution in subsequent extractions were synthesized mainly prior to the introduction of glycine-$C^{14}$ and therefore unlabeled proteins prevail in them.

At this stage collagen radioactivity is also low. With the passage of time the radioactive procollagen obtained in the first extraction, being transformed into collagen through intermediate stages, causes the enrichment of these proteins in radiocarbon. This transformation, as well as the continuous elimination of carbon-14 from the organism without any intake from outside, results in the fact that the synthesis of new portions of collagen is accompanied by the incorporation of a gradually diminishing quantity of radiocarbon. The formation of unlabeled protein which dilutes the formerly synthesized radioactive procollagen causes a decrease in its radioactivity; 40 days after the injection of glycine we see that the radioactivity of the

Table 1. Radioactivity of collagen and procollagens from successive extracts of skin of normal guinea pigs as a function of time elapsed since single injection of glycine-$C^{14}$ (disintegrations per minute per 10 mg of protein).

| Proteins | No. of hours after injection | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 3 | 3 | 6 | 6 | 12 | 12 | 24 | 24 | 96 | 96 | 480 | 840 | 840 | 960 | 960 | 960 | 960 | 960 | 960 |
| Procollagens: | | | | | | | | | | | | | | | | | | | |
| Extract 1 | 71 | 52 | 119 | 99 | 150 | 100 | 157 | 180 | 97 | 71 | 64 | 32 | 18 | 18 | 7 | 8 | 6 | 16 | 18 |
| Extract 2 | 62 | 45 | 114 | 86 | 110 | 82 | 119 | 124 | 75 | 58 | 59 | 44 | 37 | 32 | 39 | 20 | 12 | 26 | 38 |
| Extract 3 | 40 | 37 | 79 | 70 | 84 | 45 | 84 | 84 | 52 | 40 | 52 | 40 | 41 | 47 | 41 | 44 | 27 | 37 | 40 |
| Extract 4 | 50 | 43 | 60 | 50 | 64 | 38 | 64 | 47 | 42 | 35 | 44 | 52 | 53 | 82 | 71 | 38 | 33 | 36 | 41 |
| Extract 5 | 35 | 32 | 65 | 44 | 60 | 30 | 64 | 53 | 53 | 37 | | 55 | 35 | 87 | 70 | | 30 | 25 | 33 |
| Extract 6 | 27 | 24 | 32 | 39 | 38 | 40 | 48 | 38 | 32 | 39 | 40 | 32 | 31 | 65 | 44 | 39 | 20 | | 40 |
| Collagen | 12 | 12 | 17 | 9 | 25 | 17 | 26 | 20 | 30 | | 40 | 50 | 42 | 108 | 80 | 53 | 44 | 43 | 46 |

procollagen of the first extraction is 7 to 10 times as low as that of collagen. At the same time the proteins isolated from the subsequent extracts still contain a considerable amount of carbon-14, which augments with the increase of the serial number of the extraction. The probability of such a transformation process is confirmed by researches carried out by other authors [Neuberger (*6*); Neuberger, Perrone, and Slack (*7*); Perrone and Slack (*8*)], who are also inclined to explain the increase in collagen radioactivity by the accumulation of the newly synthesized, "young" collagen. At present we cannot define the nature of the difference between these transient forms of procollagen. It might be that they differ in the degree of intermolecular interaction of individual primary particles in the connective tissue.

## Procollagens in Alkaline and Neutral Salt Solutions

At this point it is necessary to mention the results of the investigations of collagen-like proteins soluble in alkaline solutions and in neutral salt solutions. For instance, Harkness, Marko, Muir, and Neuberger (*9*) found that the incorporation of glycine carbon-14 in alkali-soluble collagen proceeds at a higher rate than in citrate-soluble collagen. A conclusion was drawn, on this basis, that alkali-soluble collagen is the actual precursor of collagen. In agreement with these data are Jackson's investigations (*10*) on collagen formation in connective tissue after a local injection of carrageenin. It was found in these investigations that collagen soluble in neutral salt solutions was again the first to form, and that the fraction of citrate-soluble collagen appeared later. The rate of glycine-$C^{14}$ incorporation in the neutral soluble fraction was much higher than in the citrate-soluble fraction and in collagen, whereas it was the same for the latter two. In this connection it should be mentioned that we investigated physicochemical properties of alkali-soluble collagen and found that these two proteins are identical with respect to glycine and hydroxyproline content, the sedimentation constant, and the intrinsic viscosity value. These proteins have very similar molecular weights and particle shapes and, consequently, do not differ from each other in principle. Alkali-soluble protein is soluble in a citrate buffer solution, too, and therefore we have encountered it in the first procollagen extracts when carrying out the experiments with radioactive glycine described above. Obviously, this protein is one of the above-mentioned transient forms of procollagen. The same holds true for the fraction soluble in neutral salt solutions.

It is worth saying a few words about the protein termed "tropocollagen"—that is, the precursor of collagen. As is known, this name was given by Gross, Highberger, and Schmitt (*11*) to structural elements of the so-called FLS (fibrous long spacing) having a length of about 3000 angstroms and discovered with the aid of electron microscopy. It is just this length that is characteristic of particles of procollagen (as well as of ichthyocol, which is similar to it) in solution, according to the results of the physicochemical investigation of these proteins in the soluble state, and to the recent electron-microscopic investigations (*12*). It should be admitted, therefore, that the terms *procollagen* and *tropocollagen* refer to one and the same protein.

## Molecular Weight and Particle Length

We have given much attention to the study of procollagen solutions by physicochemical methods. In the first place we were interested in the molecular weight of procollagen and in the shape of its molecules. At one time it was believed that the molecular weight of procollagen is 70,000 and its particle length is 380 angstroms, the degree of asymmetry being around 1/20. Such data were obtained by Bresler *et al.* (*13*) on the basis of studies of the sedimentation and diffusion of this protein. As was discovered later, these data are not applicable to native procollagen, since procollagen was dissolved at about 40°C—that is, under conditions where this protein is entirely denaturated and breaks up into constituent parts. Therefore the molecular weight 70,000 applies rather to the degradation products—that is, to the so-called parent gelatin.

In this connection we undertook investigations with the aim of determining the molecular weight of native procollagen. We have studied the sedimentation, diffusion, and viscosity of procollagen dissolved in a citrate buffer solution with *p*H 3.7, containing either 1 percent calcium chloride or 0.5*M* urea. The latter two substances were added in order to prevent spontaneous coagulation of procollagen on the boundary, which was frequently observed in studying diffusion when only citrate buffer solution was used as a solvent. We obtained the sedimentation constant ($s = 3.05$ to 3.25 Svedberg units), the diffusion constant ($D = 0.35$ to $0.40 \times 10^{-7}$ cm²/sec), and intrinsic viscosity ($[\eta] = 16$ to 17). The respective coefficients were determined at the lowest concentrations possible and extrapolated graphically to infinite dilution. One of the determinations of the diffusion coefficient was, for instance, made at a protein concentration of about 0.02 percent by means of a polarization interferometer.

On the basis of these data we calculated the molecular weight of procollagen (about 700,000) and its particle length (approximately 6000 angstroms). The difficulties we faced in studying collagen solutions, which were caused by

the extremely high degree of asymmetry of this protein, did not permit us to regard these values as precise. As we learned later, other investigators simultaneously studied the molecular weight of procollagen and similar proteins (for example, ichthyocol). It is interesting to note that they obtained identical sedimentation constants (about 3 Svedberg units) and intrinsic viscosity values (about 15). This signified that the molecular weights and the sizes of these molecules should be approximately the same. However, greatly varying values for molecular weight were obtained. Very high values exceeding one million were obtained by the light-scattering method. Such data should be treated with some caution, for it is quite difficult to clarify solutions of these proteins from dust, the presence of which heavily distorts the results. Noda (*14*) obtained data similar to ours for soluble collagen from a rat tail ($s = 3.5$ Svedberg units; $D = 0.5 \times 10^{-7}$ cm²/sec; $M = 700{,}000$). Peng Chia-Mu and Tsao Tien-Chin (*15*) found the molecular weight of procollagen to be equal to 400,000, using the osmometry method.

In our judgment, the most thorough investigations appear to be those carried out by Boedtker and Doty (*16*) who found a convenient way to remove dust from solutions and who measured the molecular weight and the particle size of ichthyocol by the light scattering, sedimentation, viscosimetry, osmometry, and birefringence methods. The results obtained by the use of these methods

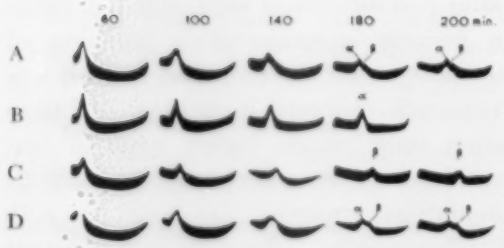


Fig. 1. Sedimentation diagrams from experiments on the isolation of the individual components of procollagen. Sedimentation was performed in a Svedberg type ultracentrifuge, at a speed of 56,000 rev/min and at a rotor temperature of about 20°C. The material was dissolved in phosphate buffer at *p*H 8, containing 10 percent of potassium thiocyanate. (*A*) Sedimentation of the initial mixture of two breakdown products of procollagen. The slower component is designated the α-component and the faster one, the β component. (*B*) Sedimentation of α-component. (*C*) Sedimentation of β-component. (*D*) Sedimentation of a mixture of α and β components in which the relative proportion of β-component was intentionally made greater than in the initial mixture.

were in good agreement. Boedtker and Doty found the molecular weight to be 350,000 and the particle length about 3000 angstroms. These values appear quite probable. However, the diffusion constant ($0.5 \times 10^{-7}$ cm²/sec) is in discord with this molecular weight. So are the data on the molecular weights and the quantitative ratio of the components resulting from the breakup of procollagen molecules under certain conditions. We shall deal with this problem later on. Meanwhile, we should like to emphasize once again that the investigation of this protein by physicochemical methods is accompanied by a good many difficulties, since procollagen solutions are far from ideal. Some errors are quite possible, but they will be corrected in the future as our knowledge of this protein is expanded.

## Denaturation

Procollagen in solution retains its native state only under certain conditions. When solutions are heated, procollagen is denaturated, that is, decomposed into its components. The denaturation of procollagen is accompanied by a decrease in viscosity and optical rotation. It should be noted that the terms *native* and *denaturated*, as employed here, may seem somewhat conventional. We apply the word *native* in the sense of "nondenaturated." We do not see any reason for not using the term *denaturation*, though in the case under study this process is not accompanied by a "classical" increase in viscosity and optical rotation characteristic for the "classical" denaturation of globular proteins. By "denaturation" we imply here "the loss of specific structure of the macromolecule without chemical degradation" (*16*).

Thus, the heating of procollagen solutions is followed by a drastic decrease in viscosity and optical rotation. This process is irreversible, just as is the transformation of collagen into gelatin, and it is to some extent similar to the thermal shrinkage of collagen. The temperature threshold of such denaturation of procollagen from rat skin depends on the nature of the medium. In a citrate buffer solution with *p*H 6, it was observed at about 40°C; with *p*H 4, at about 37°C; with *p*H 2, at about 30°C. The addition of urea to the citrate buffer solution with *p*H 4 elicited a marked reduction of the threshold of denaturation (30°C at 3*M* and 23°C at 6*M*). Guanidine chloride, potassium thiocyanate, calcium chloride, and so on, had the same effect. On ultracentrifuge stud of a procollagen preparation in a citr buffer solution with *p*H 3 + 3*M* u which was preheated for 10 minutes 30°C, we discovered two peaks on sedimentation diagrams.

The pretreatment conditions and abrupt reduction in viscosity of the so tion without a considerable change in sedimentation coefficients indicated th in this case, there takes place the deco position of the procollagen molecu into individual components as a result the rupture of hydrogen and, perhap salt bonds. We also observed two peak on the sedimentation diagrams for d natured ichthyocol and soluble collage from codfish skin. This permits us to b lieve that such a two-component natur is a common characteristic of the stru ture of all the proteins of the collage group. Such an opinion was also e pressed by Doty in his letter to us. It remarkable that the behavior of procol lagen in solutions—namely, the chang in its properties on denaturation—i similar to the process of denaturation desoxyribonucleic acid in solutions. I the latter case the viscosity also decrease at a certain temperature, hydrogen bond are also ruptured. In this respect the in vestigation of the process of the denatura tion of procollagen and of the decom position products of this protein is o interest not only as a solution of a par ticular problem but, possibly, also o more general problems pertaining to th principles of building of biologically im portant fibrillar formation.

## Isolation of Components

Our further objective was the isola tion of the above-mentioned component Since these components resemble gelati with respect to a number of properties we applied some methods employed in gelatin fractionation. We attempted to carry out separation by the alcohol method, by precipitation with ammo nium sulfate, and by using sodium do decyl sulfate. But we never achieved the desired results. At best, we obtained one component with a lower content of the other, as compared with the initial mix ture. At last we succeeded in working out a technique yielding satisfactory results The technique consisted in precipitating components from their solution in 5*M* urea by adding an ammonium sulfate solution at 37°C. The faster component designated the β-component, was the firs to precipitate; then, as the concentration of ammonium sulfate increased, the

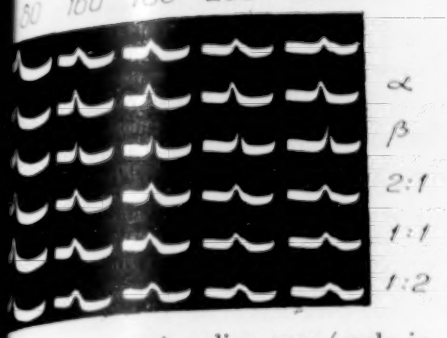


Fig. 2. Sedimentation diagrams (scale in minutes). (Top) Initial component mixture after denaturation of procollagen. (α) Isolated α-component. (β) Isolated β-component. (2:1, 1:1, and 1:2). Sedimentation diagrams of artificial mixtures of α- and β-components in weight ratios 2:1, 1:1, and 1:2, respectively.

lower component, designated the α-component, separated out. On subsequent reprecipitations, rather pure preparations (as judged by the respective sedimentation diagrams) were obtained. To prevent a possible aggregation, we examined these components in a solution containing 10 to 20 percent of potassium thiocyanate.

Figure 1 shows sedimentation diagrams. The first row represents initial mixture sedimentation; the second, α-component sedimentation; the third, β-component sedimentation; the fourth, the sedimentation of an artificial α–β component mixture. In the latter case the quantitative ratio of these components is changed as compared with the initial mixture. Figure 2 demonstrates similar sedimentation diagrams of experiments undertaken with a view to establishing the quantitative α/β weight ratio in a procollagen molecule. Here, as well as in Fig. 1, the first row corresponds to the initial component mixture after procollagen denaturation in 5*M* urea at 37°C; the second row represents the isolated α-component; the third row, the β-component; the remaining rows represent sedimentation diagrams of artificial α–β component mixtures with known weight ratios. The comparison of diagrams of the artificial mixtures with those of the initial "natural" mixture indicates that the α/β weight ratio in a procollagen molecule is 1:1.

## Nature of Components

Now we should like to make a brief excursion into the nature of these components by saying a few words about the doubts that occurred to us and that may occur to others. The basic problem was whether these components are various structural elements of the procollagen molecule or whether they represent different degrees of aggregation of one and the same substance. We believe them to be various structural elements. Their release takes place under conditions that cause a rapid rupture of all the hydrogen type bonds. Under such conditions, the preservation of particle aggregates linked by hydrogen bonds is most unlikely.

We observed two components in the sedimentation of procollagen pretreated by heating and with high concentrations of thiocyanate or urea at room temperature. Thus, different treatments produce identical effects, and this points to the rupture of nonvalence bonds in all these cases. The possibility of separating the components by means of ammonium sulfate shows that they are of different nature. Finally, according to the preliminary data, hydroxyproline content of the β-component is lower than that of the α-component.

All these data indicate that in this case we are dealing with various structural elements of the procollagen molecule and not with a monomer or dimer (or polymer), or with the products of an irregular cleavage (*17*).

## Conclusions

Now we shall dwell briefly on the results of studying the sedimentation and diffusion of these components. A phosphate buffer solution with *p*H 8, containing 10 percent of potassium thiocyanate, was used as a solvent in these experiments.

We have found the sedimentation constant (4 Svedberg units) and the diffusion constant ($2.6 \times 10^{-7}$ cm²/sec) for the α-component and the respective values for the β-component ($s = 5.7$ Svedberg units and $D = 1.6 \times 10^{-7}$ cm²/sec). These data were obtained by extrapolation to infinite dilution of protein in solution. The molecular weights calculated on the basis of these values proved to be equal to 125,000 and 290,000 for the α and β components, respectively. It should be remarked that the measurement of the diffusion coefficients has not always led to reproducible results, especially in the case of the β-component. Taking this into consideration, we are not quite sure of the precision of the molecular weights obtained. These values may be somewhat exaggerated, due to the tendency of the component particles to aggregate.

Recently we had an opportunity of getting acquainted with a paper by Doty and Nishihara read at the conference devoted to the recent advances in gelatin and glue research, held at the University of Cambridge, July 1957. In this paper some relevant data are presented. It is shown that the molecular weight of soluble collagen (or, as we call it, procollagen) of calf skin is 360,000 and its particle length is 3300 angstroms. On denaturation, it decomposes into components having molecular weights of about 120,000 and 230,000. These molecular weights are close to those obtained by us for the α and β components of procollagen from rat skin. However, there is a great difference here in the calculations of the molecular weight of the initial protein on the basis of molecular weights of the components. Indeed, Doty admits that the molecule of soluble collagen from calf skin may contain one particle of one component and one particle of the other. But if our data on the quantitative ratio of the α and β components are correct, and if the structures of the molecules of procollagens from rat and calf skin are similar, then there must be a mistake somewhere, as the molecular weight of the initial protein should be equal to about 500,000 and not to 360,000. It seems to us that the results of the experiments on the determination of the quantitative ratio of the components are sufficiently clear and convincing. It means that some or other of the molecular weight values should be checked. Such discrepancies once again emphasize the difficulties associated with study of these proteins.

The data on the sedimentation and diffusion constants of the α and β components enabled us to estimate the degree of asymmetry. Here we found a value of 1/30 for the α-component and 1/50 for the β-component. Certainly, the process of denaturation itself, as well as the presence of a large amount of thiocyanate in the solution, greatly changes the configuration of the components as compared with their state in the original molecule. Nevertheless, these data enable us to make an assumption that the α and β components in the procollagen molecule are linked side by side, so that the total length of two particles of the α-component is equal to the length of a β-component particle. The two-chain model is in better agreement with this supposition. But the two-chain structure is not in accord with conceptions that arise from x-ray structural investigations —that is, conceptions of the three-chain structure of collagen. Not being specialists in the field of structural chemistry and physics, we are not in a position to

discuss this point. So far, we do not possess a sufficient number of facts about the α and β components to advance any definite hypothesis as to their position in the structure of procollagen—that is, to speak about the latter's structure.

We hope that the further study of procollagen will enable us to answer many questions concerning the structure and transformation of this protein (*18*).

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# Hemoglobin Standard

## This is the second and final report on a proposal to establish a certified standard for general use.


Division of Medical Sciences,
National Academy of Sciences–National Research Council


In 1953 the Hematology Study Section of the National Institutes of Health requested the Division of Medical Sciences of the National Academy of Sciences–National Research Council to explore the possibility of establishing a hemoglobin standard for general use throughout the country. In response to this request, the Division, in 1954, organized an Ad Hoc Panel for the Establishment of a Hemoglobin Standard under its Subcommittee on Blood and Related Problems.

George Cartwright (School of Medicine of the University of Utah) accepted the chairmanship of the panel. Its members were David L. Drabkin (University of Pennsylvania Graduate School of Medicine); William H. Crosby, Jr. (Walter Reed Army Institute of Research); George Brecher (National Institutes of Health); Wallace Brode (National Bureau of Standards); Israel Davidsohn (Mt. Sinai Hospital, Chicago), representing both the College of American Pathologists and the American Society of Clinical Pathologists; and A. H. Neufeld, representing the National Research Council of Canada. In 1956 John Gould succeeded Brode, and in May 1957, Bradley E. Copeland (New England Deaconess Hospital, Boston) and Donald Brown (Hackensack General Hospital) succeeded Davidsohn as representatives of the College of American Pathologists and the American Society of Clinical Pathologists, respectively. The panel was also fortunate in having the cooperation of E. J. King of the Postgraduate Medical School of London, who has given his full support to this undertaking.

### Routine Methods

Most routine methods of clinical hemoglobinometry depend upon the photometric measurement of a blood sample after quantitative conversion of the hemoglobin which it contains into one or another of its derivatives. For the standardization of such a procedure there is needed a color standard which, when measured in the photometer and cuvette in routine use, will establish the relation between instrument reading and concentration of the particular hemoglobin derivative. This relation can then be used in converting instrument readings for unknown samples of blood to concentration of hemoglobin by the use of Beer's law or by construction of a calibration curve.

The problem, however, is complicated by the fact that several methods of analysis involving conversion to different forms of hemoglobin are in common use. Each of these methods should have its own standard. Since a multiplicity of standards is neither desirable nor practicable, the panel decided, early in its deliberations, to select only one method of analysis, for which a suitable direct standard would be developed. It should, however, be pointed out that this procedure does not preclude the use of the standard for the indirect calibration of another method. All that need be done is to construct a calibration curve based on the measurement of a small series of normal blood samples by the standardized method and also by the method which the analyst prefers to adopt for routine use.

In the opinion of the panel, the most significant contribution which could be made to the refinement of clinical hemoglobinometry would be the widespread adoption of a single method of analysis. Failing this, the indirect calibration of other methods with the chosen method offers the only simple photometric means for the comparison of data. The procedure, however, is subject to error if the blood sample contains significant amounts of certain of the abnormal forms of hemoglobin. For example, methemoglobin and carbon monoxide-hemoglobin are


This article was prepared by the staff of the Division of Medical Sciences, National Academy of Sciences–National Research Council. R. Keith Cannan is chairman.

antitatively convertible to cyanmethe-
globin but not to oxyhemoglobin.

The panel reviewed the several photo-
tric methods in current use and came
the conclusion that the procedure in-
ving the measurement of hemoglobin
cyanmethemoglobin was the most
mising. It offered the following ad-
ntages:

1) A simple and accurate procedure
been devised by Drabkin (*1*) involv-
the addition of a single reagent to the
mple of blood.

2) The method has been adopted by
U.S. Army after extensive field
ials (*2*).

3) All forms of hemoglobin likely to
cur in circulating blood, with the ex-
ption of sulfhemoglobin, are deter-
ined by the method.

4) The color is suitable for measure-
nt in filter-type photometers as well
in narrow band spectrophotometers
cause its absorption band in the region
540 mμ is broad and relatively flat.

5) The U.S. Army has had extensive
perience in the use of solutions of
anmethemoglobin as direct standards
d has found these to be satisfactory
). The U.S. Army standards have re-
ained unchanged in optical density for
tended periods when stored at refrig-
ator temperatures, provided bacterial
ntamination was avoided.

## ield Trials

On the basis of this evidence, the
anel decided to develop a certified solu-
on of cyanmethemoglobin as a standard
nd to promote an extensive field trial
its suitability (*3*). A preliminary re-
ort of its recommendations and plans
ppeared in a number of scientific and
chnical journals in 1955 (*4*). This re-
ort outlined recommendations of the
anel, described arrangements for the
reparation and distribution of certified
tandard solutions of cyanmethemoglo-
n, and invited cooperation in an ex-
nsive field trial of the use of the stand-
rds and of the recommended method
analysis.

More than a thousand laboratories
olunteered to cooperate in the trial
ponsored by the National Research
ouncil. Distribution of the standards
as made with the assistance of the
ollege of American Pathologists, the
ational Association of Clinical Labora-
ories, the Walter Reed Army Institute
Research, and the National Research
ouncil of Canada. The laboratories re-
eived not only descriptions of the pro-
cedures for the use of the standards to calibrate photometers but also directions for the routine determination of hemoglobin in the form of cyanmethemoglobin.

The results of the study were most gratifying. The need for, and the ready and grateful acceptance of, a simple method for the standardization of hemoglobinometers was apparent. The recommended method of analysis was likewise well received. At the onset of the field trial study, only 7 percent of the cooperating laboratories had been determining hemoglobin as cyanmethemoglobin. At the time of the last report, two-thirds of the cooperating laboratories were using this method.

In the first field trial, the standard solutions were prepared from crystalline hemoglobin by David Drabkin. Three solutions in carefully determined concentrations of approximately 60, 40, and 20 mg, respectively, of hemoglobin per 100 milliliters were distributed. The optical densities of the final solutions were independently confirmed, and a continuing control on stability was maintained in the laboratories of Brecher, Gould, Crosby, King, and Neufeld. Agreement having been reached on the optical density values, the hemoglobin concentrations of the standards in milligrams per 100 milliliters were computed from the optical densities; it was assumed that the extinction coefficient of cyanmethemoglobin per milligram atom of iron (55.85 mg) per liter is 11.5 and that the pigment contains 0.335 percent of iron.

Two problems were encountered during the course of the field trial study. The first of these was the growth of certain microorganisms observed in some samples in spite of the presence of cyanide. This made it necessary to prepare and to maintain the solutions under sterile conditions. The second problem was a change, unpredictable in degree and not reported by all checking laboratories, of 2 to 6 percent in the optical density six to nine months after distribution of the standard. Samples from each lot were found to have undergone varying degrees of change—mostly fading, which was compensated for in some samples by a comparable increase in turbidity. The standards prepared and distributed by the U.S. Army in its earlier field trial had remained unchanged in optical density for three years. Inasmuch as these solutions had been prepared directly from whole blood or from washed red cells, it was suspected that the manipulation involved in the preparation of the crystalline hemoglobin for the National Research Council standards might have reduced the stability of the pigment. Therefore, a new standard was prepared from washed cells. The new standard was further modified by increasing the concentration of cyanide, since some previous preparations with such higher concentrations had shown greater stability and since the growth of most organisms would be limited by the higher concentration of cyanide.

Since the percentage change in optical density of the first standards was greater with increasing dilution of the hemoglobin pigment, and since cyanmethemoglobin solutions follow Beer's law, the second standard was distributed in only the most concentrated (60 mg of hemoglobin per 100 milliliters) of the three dilutions.

The second group of standards, modified as outlined above, was distributed in July and August of 1956. Their stability was determined in the laboratories of Drabkin, Brecher, Gould, and Crosby. The stability was satisfactory for at least nine months from the time of preparation, no change of more than 2 percent in optical density being observed.

The members of the panel have concluded that solutions of cyanmethemoglobin, when prepared, calibrated, and handled properly, are acceptable as standards for hemoglobinometry. They recognize that such standards are not ideal in all respects. However, until better standards can be developed, they are of the opinion that the availability of this reagent will greatly simplify the calibration of hemoglobinometers and will greatly increase the accuracy of hemoglobinometry.

Finally, they encourage further independent investigation in the hope that an even better standard may be developed, particularly one with improved stability and more certain maintenance of sterility.

The National Research Council's supplies of the standard cyanmethemoglobin solution are now exhausted, and no further production is planned under the auspices of the National Academy–Research Council. However, standards are now available from several commercial sources. The NAS–NRC has recommended the establishment of a program of certification of commercially produced cyanmethemoglobin standards for determining conformance with the specifications it has established. In response to the need for the establishment of such a program, as defined by the NAS–NRC, the College of American Pathologists has arranged for certification through the fa-

cilities of the laboratory of the American Medical Association in Chicago. On the basis of data obtained through this laboratory, the College of American Pathologists will certify whether commercially produced standards which have been submitted comply with the specifications established by the NAS–NRC. All users are urged to insist that the cyanmethemoglobin standards they purchase commercially carry the certification label of the College (*5*).

Detailed instructions for the preparation of the standards have been published by Crosby (*6*). Producers of the standard or instrument manufacturers may obtain technical details on the adaptation to and use of the standard in the various hemoglobinometers by writing to the Division of Medical Sciences of the National Research Council.

### Final Recommendations

The final recommendations of the National Research Council Ad Hoc Panel on the Establishment of a Hemoglobin Standard are as follows:

1) That cyanmethemoglobin be adopted as a standard in clinical hemoglobinometry.

2) That the standard be characterized spectrophotometrically on the basis that the extinction coefficient of 1 milligram atom of iron ($c = 1$ mg atom of iron per liter, $d = 1$ cm) in the form of cyanmethemoglobin at a wavelength of 540 mμ is 11.5.

3) That 0.338 percent (weight per weight) be accepted as the iron content of hemoglobin (molecular weight of 16,-$5\overline{20}$ per gram atom of iron) in accordance with the recent recommendation of the Protein Commission of the International Union of Pure and Applied Chemistry, and that a factor of $1{,}65\overline{2}$ be used in calculating hemoglobin in milligrams per 100 milliliters from millimoles per liter.

4) That the standard be distributed as a single concentration of not less than 55 mg of cyanmethemoglobin per 100 milliliters.

5) That solutions be distributed in brown glass containers and in sterile condition.

6) That, for the present, solutions be used as standards for a period not to exceed nine months from the time of preparation. This dating period is based upon the results of the National Research Council field trial. As experience accumulates with commercially prepared samples, an extension of the dating period may well be found to be justifiable.

7) That the standard be prepared from either crystalline hemoglobin or washed erythrocytes.

8) That commercial producers of the standards submit representative specimens from each lot to the College of American Pathologists, Prudential P... Chicago 1, Illinois, for certification ... that the concentration of cyanmethe... globin is within ± 2 percent of the v... stated on the label; (ii) that the solu... is substantially optically clear; and ... that it is microbiologically sterile ...

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# News of Science

### Research Based on Sputniks I and II Reported by Soviets

On 19 May the Soviet Embassy in Washington released an article on "Soviet artificial earth satellites" that presents in popular form some of the results of the experiments that Russian scientists are conducting in connection with the first two sputniks. The article, which is based on material published in *Pravda* on 27 April, states that fuller accounts of these results will soon appear "as scientific papers in various journals." Following are excerpts from the article.

"*Radio and optical observations of the sputniks.* Since an analysis of the changes in a sputnik's orbit as regards time makes it possible to estimate the density of the upper layers of the atmosphere, studies of the movements of sputniks are of great significance. The elements of a sputnik's orbit can be determined by tracking it by radiotechnical and optical methods.

"The radiotechnical methods included radio direction-finding and observations of the Doppler effect during the reception of radio signals from the sputniks. The Doppler effect is a result of the fact that the frequency of signals receiv... increases as the object on which t... radio transmitter is installed dra... nearer to the receiving point. T... changes in the frequency depend on t... speed at which the object draws near... or moves away. In the case of a sputni... the speed at which it draws nearer t... or moves away from, the receiving st... tion on the ground is so great that t... Doppler effect can not only be observ... on an ordinary radio set, but can al... be used for registering the moment th... sputnik passes at the distance clos... from the point of observation and al... for measuring the distance to the spu... nik and its velocity.

"During radio observations of the si... nals of Sputniks I and II, the frequenc... of the signals received were measur... by special radio equipment, including ... recording chronograph.

"To obtain greater accuracy of mea... urement observations were conducted ... signals at frequencies of 40 megacyc... per second, which are less subject to th... influence of the ionosphere. The pow...

the transmitters ensured the definite ception of the signals within the entire ne of direct visibility. Six or seven ssages of the sputnik over the ground ations could be observed consecutively uring the course of 24 hours.

"To analyze the radio signals received, a method was worked out making it possible to determine with a precision of 0.1–0.2 seconds the moment which the sputnik passes at the shortest distance from the observation point. "The observations have confirmed hat the Doppler effect can successfully e employed for determining the paramters of the sputnik's orbit. Simplicity nd dependability of the equipment are istinctive features of this method. By ising the frequency of the transmitter nstalled on a sputnik and by automatic egistration of the frequencies the errors f this method can be substantially reuced.

"The most simple method of optically racking the sputniks was by registering he moment of their passage over the bservation point.

"For a more precise determination f the bearings, special methods were mployed; modernized aerial cameras ere used for obtaining photographs of he track of the sputnik. The time durng the filming was marked by several onsecutive openings and closings of the hutter, and the timing registered by a hotoelectric method. In this way a disinct track of the sputnik was visible on he photograph. A high degree of preision was obtained when using such ameras.

"A method of photography with highly-sensitive equipment has been worked out in tracking the artificial satellites. Very promising among these are electronic-optical transformers. The new method makes it possible to track the sputniks without the use of large optical systems, greatly simplifying the equipment necessary for observation.

"*Determination of the density of the atmosphere.* . . . The density of the atmosphere declines sharply as the distance from the earth's surface increases. That is why the force of resistance is unequal at different sections of an elliptical orbit. With a sufficiently elongated orbit the force of resistance in the perigee is much greater than in the apogee. Hence, the main deceleration takes place in the area of the perigee. Such a nature of varying deceleration results in the height of the apogee declining much faster than that of the perigee. A sputnik's elongated orbit changes so that its shape gradually becomes more of a circle.

"After the launching of the first sputniks optical observations and radio tracking made it possible to trace the evolution of their orbits. Since the action of the atmosphere on the sputnik on separate sections of its orbit is very small, scientists so far have not succeeded in measuring local deceleration. All data of the orbits immediately after the launching of the sputniks and also the changes in the periods from revolution to revolution throughout their life were measured on the basis of the observations of the first Soviet earth satellites with a precision sufficient for definitely determining the density of the atmosphere.

"The speed of change in the period of revolution greatly depends both on the density of the atmosphere in the perigee area and also on the speed with which the density declines as the altitude increases. The speed in the drop of the density is characterized by a parameter called the "height of uniform atmosphere," which is directly proportional to the temperature of the atmosphere and inversely proportional to its molecular weight.

"On the basis of a theoretical analysis of the results of the observations scientists succeeded in definitely determining the value of the product of the density of the atmosphere and the square root of the 'height of the uniform atmosphere' at altitudes of the perigees of the first sputniks (225–228 kilometers). The values of the density were calculated for definite theories regarding the value of the 'height of a uniform atmosphere.' The obtained value of density proved to be five to ten times greater than the values of density at these altitudes indicated in a number of models of the atmosphere built on the basis of rocket measurements prior to the launching of the sputniks. It should be noted that determination of the density by a study of the purely mechanical action of the atmosphere on the sputnik is quite exact.

"The atmosphere is not the same over various areas of the earth's surface. At the same altitudes the density and temperature change, depending on the latitude and time of day, which in turn is related to the unequal heating of the upper atmosphere by ultraviolet, x-ray and minute-particle radiations of the sun.

"As a result of the fact that the gravitational field of the earth differs from the central one, the orbits of the sputniks changed their position in space. Thus, for the first Soviet sputniks the angular distance of the perigee from the midday meridian changed approximately by 4 degrees and the latitude of the perigee changed by 0.35 degrees in 24 hours.

"Inasmuch as the main action of the atmosphere occurs in the perigee area of the orbit, the change of its position leads to a change in the value of deceleration. This makes it possible to estimate the value of the changes in the state of the atmosphere depending on the latitude and time of day.

"Calculations to determine the density of the atmosphere, taking into account the changes in the location of the perigee of the orbit, were made on the basis of observations of the first sputniks. The calculations showed that the product of the density and the square root of the 'height of uniform atmosphere' increases as the orbit passes from the night side of the atmosphere to the day side and reaches its maximum at noon. An analysis of deceleration also revealed a decline of this value during the passage from the more northerly regions into those of the equator. Mention should also be made of the fact that there is good coincidence in the values of densities calculated on the basis of observations of Sputniks I and II and the carrier-rocket of Sputnik I.

"The data obtained provide grounds for the conclusion that the temperature of the atmosphere at altitudes around 225 kilometers is higher than was formerly supposed on the basis of theoretical considerations. The discovery of higher temperatures of the atmosphere confronts geophysicists with the problem of the powerful sources of energy which heat the atmosphere. The known ultraviolet and x-ray radiation of the sun is hardly sufficient for that. At present only various hypotheses can be advanced. It may be assumed, for example, that the upper atmosphere in the Arctic regions is intensively heated by solar radiation of minute particles. It is possible that in general the entire upper atmosphere is additionally heated either by infrasound waves coming from the troposphere or by electric currents arising in the electrically-conductive ionized air as a result of its movement in the earth's magnetic field. . . .

"*Results of ionosphere exploration.* . . . Observations of the propagation of radio waves of various frequencies emitted by the sputniks at different altitudes are a new means of exploring the outer ionosphere.

"In receiving radio signals from the first sputniks at a frequency of 40 megacycles their 'radio dusk' and 'radio dawn' were fully observed in a number of cases and their respective time was recorded. In contrast to the optical dawn or dusk of a sputnik, which are characterized by the fact that at this moment the beam of light from the sputnik to the observer comes in a straight line, the radio beam at 'radio dawn' or 'radio dusk' is deflected in the ionosphere.

"Because of this, 'radio dusk' occurs later than optical dusk and conversely, 'radio dawn' precedes optical dawn. The difference in time between optical dawn and 'radio dawn' (or optical dusk and 'radio dusk') makes it possible to determine the magnitude of the deflection of the radio beam. Since the deflection of the radio beam in the ionosphere depends on the change in electron concen-

tration with altitude, it is possible, by assuming a certain law of the change of electron concentration, to calculate theoretically its magnitude at different altitudes. In doing so the influence of the lower strata of the ionosphere can be estimated on the basis of direct measurements carried out by a network of ground stations.

"The data obtained from observation of the radio signals from the first sputniks make it possible to consider that electron concentration in the outer ionosphere (above the chief maximum) decreases with the rise of altitude 5 to 6 times slower than it increases below the maximum. Thus, from an altitude of 100 kilometers to an altitude of 300 kilometers the electron concentration mounted during the period of observation (in October) approximately tenfold, and from an altitude of 300 kilometers to 500 kilometers it dropped by half.

"It should be noted that similar changes in electron concentration with the rise of altitude were also registered in launching a Soviet high-altitude rocket, which was reported in *Pravda*. In this experiment electron concentration at a height of 473 kilometers was of the order of 1,000,000 electrons in a cubic centimeter.

"*Study of cosmic rays.* For studying cosmic radiation Sputnik II was equipped with two instruments for registering the number of particles of this radiation. Circling the earth, the sputnik traveled at different distances from its surface. That is why measurements of the cosmic rays on the sputnik made it possible to ascertain the dependence of the number of particles on altitude. An analysis of the material obtained has revealed that the intensity of cosmic radiation increases by approximately 40 per cent from the minimal height of the orbit (225 kilometers) to an altitude of 700 kilometers. This increase is due primarily to the fact that the screening effect of the earth diminishes as altitude increases, and the cosmic rays are able to reach the instrument from a great many directions.

"The earth's magnetic field also creates an obstacle to cosmic radiation reaching the earth. Deviation of the particles of cosmic beams in the earth's magnetic field results in the fact that only particles whose energy exceeds a certain value can reach every point on the earth's surface in a definite direction. Naturally, the farther away we go from the earth, the weaker the magnetic field becomes, and the smaller is its effect upon the cosmic rays. Calculations show that the cosmic ray intensity increasing with altitude as measured in the flight of the sputnik can be explained by the above-stated reasons.

"A study of cosmic rays through instruments installed in a sputnik may also reveal the dependence of the intensity of cosmic rays on latitude and longitude. This makes it possible to obtain new information about the earth's magnetic field. Measurements of the magnetic field on the surface of the earth give an idea about the character of terrestrial magnetism and allow to foretell what the magnetic field should be at great distances from the earth. Proceeding from this it is possible to calculate the expected distribution of the intensity of cosmic rays over the earth's surface. Specifically, it is possible to indicate the lines of the constant intensity of cosmic rays (isocosm). Measurements of cosmic rays made during the flight of the sputnik have shown that the lines of constant intensity obtained experimentally and calculated theoretically differ substantially. This result is in good agreement with the conclusion of the American physicist, Simpson, who organized a large series of flights of high-altitude aircraft over the equator. They showed that the equator determined by means of cosmic rays does not coincide with the geomagnetic equator.

"Consequently, there is a considerable divergence between the characteristics of the earth's magnetic field obtained by means of cosmic rays, on the one hand, and by measuring the magnetic field on the surface of the earth, on the other. These divergences are due to the fact that the trajectories of cosmic rays are determined by the magnetic field at very high altitudes, while direct measurements characterize the magnetic field near the surface of the earth. Cosmic rays make it possible to 'sound' the earth's magnetic field at great distances from the earth, permitting a new approach to the study of the earth's magnetic field and the system of electric currents in the upper atmosphere.

"Observation of cosmic rays with the aid of sputniks have made it possible also to register variations in the intensity of this radiation. These variations are, obviously, connected with the condition of the interplanetary environment near the earth. One instance of a sharp increase (by 50 per cent) in the number of particles of cosmic radiation was registered. At that time, however, ground stations did not detect any essential increase in the intensity of cosmic radiation, and this event is now being studied in detail. It is possible that it was caused by the sun's generation of particles of low-energy cosmic rays (which are strongly absorbed by the earth's atmosphere) or by the sputnik passing through streams of high-energy electrons (connected with the minute-particle radiation of the sun). . . .

"*Biological investigations.* . . . Of great interest is the behavior and condition of the test animal in the most difficult, from the biological viewpoint, stage of the sputnik's flight—in its launching and entry into orbit. On its ascent to the orbit the sputnik traveled at an accelerated pace, the acceleration exceeding many times that of gravitation on the surface of the earth, and the seeming weight of the animal increasing with the acceleration.

"During the ascent the animal [Laika] was in a position for the acceleration to act on it in the direction from the chest to the back, which pressed the animal to the floor of the chamber. This position of the animal was chosen because it is a most favorable one for the organism. Simultaneously with acceleration the vibration and noise of the rocket engine reacted on the animal during the ascent.

"The behavior and condition of the animal during the sputnik's ascent to the orbit was registered quite fully. The information obtained indicates that the animal withstood the increase in its seeming weight and continued to move its head and body freely only until a certain point of the acceleration. After that the animal was pressed to the floor of the chamber and no more or less noticeable movements were registered.

"A study of the data obtained from the sputnik showed that immediately after the launching, the frequency of the heart contractions approximately trebled as compared with the initial frequency. The electrocardiograms have not revealed any morbid symptoms. They showed a typical picture of quickened heart-beat, the so-called sinus tachycardia. Later on when the effect of the acceleration not only continued but mounted, the heart-beat frequency diminished.

"One can easily imagine that as the seeming weight of the animal increased the respiratory movements of its thorax became difficult, breathing became more shallow and frequent. Indeed, telemetric recordings show that in the sputnik's ascent to its obrit, the animal breathed three to four times as fast as it did at the beginning.

"There is reason to assume that the changes observed in the condition of the animal's physiological functions owe their origin to the sudden action on the organism of sufficiently strong external irritants: acceleration, noise and vibration, which began at the launching and continued on the ascent. An analysis of the data obtained and their comparison with the results of preceding laboratory experiments indicate that the animal withstood the flight quite well from the launching to the entry of the sputnik into orbit.

"After the sputnik got into orbit, the centrifugal force acting upon it balanced the earth's attraction, and a state of weightlessness set in. In this condition the animal's body ceased to press upon

chamber's floor, and by contracting muscles of its extremities it easily shed itself off the floor. The recordrs suggest that these movements were ief and rather smooth.

"As the animal's thorax was no longer ssed under the influence of its inreased weight, the frequency of its eathing declined. After a very brief eriod of quickened heart-beat, the sysle frequency continued to diminish, nsistently approached its initial level. took, however, about three times as g for the number of heart beats to ach the initial level as it did in laborary experiments in which the animal as subjected to the same acceleration when the sputnik was put into orbit.

"This is most probably connected with he fact that in the ground experiments he animal, after the acceleration ended, as in normal conditions, while in the putnik the acceleration was replaced by state of complete weightlessness.

"In this state the animal's nerves hereby it feels the position of its body space were not sufficiently affected by he external irritants. This conditioned he change in the functional state of the ervous system regulating blood circulaion and respiration and determined a ertain extension of the time for the noralization of these functions after the cceleration effect ended.

"It is also possible that this phenomenon was somewhat intensified by the ction of concomitant factors during the scent—vibration and noise, which were reater than in the laboratory experiments.

"It should be noted that the change in he physiological functions, registered in he animal at the beginning of the sputnik's movement along its orbit, coincides asically with the results of previous nvestigations with high-altitude rockets.

"An analysis of an electrocardiogram ecorded during the state of weightlessness revealed certain changes in the conguration of its elements and the duraion of separate intervals. The observed hanges were not of a pathological naure and were connected with the heightened functional activity during the eriod preceding the state of weightlessness. The electrocardiogram showed ransient reflected nervous changes in he regulation of the heart's action. In he subsequent period the picture of the lectrocardiogram grew increasingly loser to that characteristic of the anial's initial condition. In spite of the nusual state of weightlessness the anial's motions were moderate.

"The normalization of blood circulaion and respiration during the period of weightlessness, *i.e.*, during the period of the sputnik's movement along its orbit, evidently indicates that this factor in itself did not cause any essential and stable changes in the state of the animal's physiological functions. Thus it may be said that the animal well endured not only the sputnik's ascent to the orbit but also the conditions of travel along the orbit.

"In ensuring the conditions necessary for the animal's vital activity in a prolonged flight in a sputnik, it is most important to provide a proper gas environment, the composition and pressure of which should not cause violations of the animal's physiological functions. This task could be accomplished only by the use of an hermetically sealed chamber in which normal atmospheric pressure with an oxygen content of 20 to 40 per cent and a carbon dioxide gas content of no more than one per cent was maintained by air regeneration.

"Special highly active chemical compounds which, absorbing water vapors and carbon dioxide, emitted oxygen were used as regenerating substances. These chemical compounds absorbed also such noxious gases formed in the process of the animal's vital activity as ammonia, for example. An analysis of the data obtained showed that oxygen was emitted in sufficient quantities. The fact that the pressure in the chamber did not drop shows that it was effectively sealed. . . ."

## Center for Communication Sciences

A Center for Communication Sciences has been set up at Massachusetts Institute of Technology to conduct studies of the communication functions of the nervous system, of computers, and of organisms and machines in conjunction with each other.

The center will use the facilities of the Research Laboratory of Electronics, where there has been a concentration of interest in this field. The steering committee for the center is composed of Jerome B. Wiesner, director of the Research Laboratory of Electronics; Claude E. Shannon, one of the originators of the mathematical theory of communication; Gordon S. Brown, head of the department of electrical engineering; Robert M. Fano, a communications engineer specializing in information theory; Roman Jakobson, a linguist; and Walter A. Rosenblith, a biophysicist with a special interest in sensory communications.

The activities of the new center can be traced back to the Massachusetts Institute of Technology Radiation Laboratory, which, during World War II, was responsible for the development of radar. After the war, the Research Laboratory of Electronics was established to continue research work in related fields on a peacetime basis. Staff members of the laboratory have worked on a large number of problems, but increasing interest in the communication sciences has resulted in the participation of research-workers from fields not commonly associated with electrical engineering, such as psychology, physiology, and linguistics.

Among the questions to which the center would like to find the answers are the following: Can we describe in mathematical form the grammar of a natural language? Can we give a rational account of the way in which the brain processes information coming to it through the senses? What role does information play in human learning and decision-making? Are there laws which resemble the laws of physics in their generality and predictive power?

## Scientific Secretaries for Atomic Energy Conference

An international team of 21 scientific secretaries from 13 countries has been appointed for the second United Nations International Conference on the Peaceful Uses of Atomic Energy, to be held in Geneva 1–13 September. All have arrived at U.N. Headquarters in New York. They will work there, and later in Geneva, on the subjects that will receive major attention at the conference: nuclear fission; fission reactor engineering; physics; biology and isotopes; and raw materials, mining, and chemistry.

The secretaries, whose appointments were announced last month by Sigvard Eklund, conference secretary-general, are: Renee Bovy (Belgium), Frank Bruce (United States), Terence E. F. Carr (United Kingdom), Thomas C. Church (Canada), Thomas Coor (United States), D. Harold Copp (Canada), Israel Dostrovsky (Israel), Aleksandr Nikitich Efimov (U.S.S.R.), Hiroshi Fukunaga (Japan), Claudio Garavaglia (Italy), Fred Hudswell (United Kingdom), David Okrent (United States), Ivan Dmitrievich Rozhansky (U.S.S.R.), Afaf A. Sabri (United Arab Republic), Carlos Sanchez del Rio (Spain), Cesar Sastre (Argentina), Gavriil Sergeevich Strelin (U.S.S.R.), Pierre Yves Tanguy (France), Ivan Ulehla (Czechoslovakia), William Brian Woollen (United Kingdom), and Valery Ziegler (France).

## News Briefs

*Revue de Géographie Physique et de Géologie Dynamique* is again being published after suspension because of World War II. For information, communicate with Masson et Cie., éditeurs, Paris.

* * *

Norman Hilberry, director of Argonne National Laboratory, is heading an atoms-for-peace survey mission to Latin America. This is the first major project

of its kind sponsored by the recently formed International Atomic Energy Agency. Hilberry's survey team includes nuclear energy and administrative specialists from France, Britain, Brazil, and IAEA.

* * *

The number of births for the first quarter of 1958 is 7000 less than in the first quarter of 1957. Population Reference Bureau, Washington, D.C., attributes this to the recession. A deficiency in births, as compared with the year before, has existed since November 1957. In 1958, the drop has been greater each month. In January 1958, it amounted to 1000 births; in February, to 2000; and in March, to 4000. This is the first time for several years that the seasonal trend in births has shown a consistent decline.

* * *

Some 80 scientists from the United States, Great Britain, and France took part in a two-day conference on communication of scientific information at the San Jose (Calif.) Research Laboratory of the International Business Machines Corporation, 26–27 May. The meeting coincided with the dedication of IBM's new research, manufacturing, and educational facilities 10 miles south of San Jose. Alan T. Waterman, director of the National Science Foundation, was the principal speaker.

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A contract for the design and operation of the Atomic Energy Commission's exhibit in the Second International Exhibition of the Peaceful Uses of Atomic Energy—a commercial exhibition—to be held in Geneva, Switzerland, 1–14 September, has been awarded to the Atomic Industrial Forum, Inc., of New York.

## Scientists in the News

JONAS E. SALK, professor of experimental medicine, University of Pittsburgh; AMOS CHRISTIE, professor of pediatrics, Vanderbilt University School of Medicine; and ALEX M. BURGESS, Providence, R.I., received awards during the 39th annual session of the American College of Physicians. The James D. Bruce Memorial Medal was awarded to Salk for outstanding accomplishments in preventive medicine; the John Phillips Memorial Medal went to Christie for research in internal medicine, especially in histoplasmosis; and Burgess received the Alfred Stengel Memorial Award for his "outstanding influence in maintaining and advancing the best standards of medical education, medical practice and clinical research."

The American Heart Association has announced the appointment of three career investigators, bringing to six the number of scientists whose research is being supported on a lifetime basis by the association and its affiliates. The new career investigators are: DAVID B. SPRINSON, professor of biochemistry, Columbia University College of Physicians and Surgeons; JOHN V. TAGGART, professor of medicine, also at Columbia; and LEWIS W. WANNAMAKER, associate professor of pediatrics, University of Minnesota Medical School.

JAMES M. MITCHELL, associate director for management and public affairs, National Science Foundation, is head of a three-man team of United States management experts who will study the organization, staffing, and training needs of agencies of the Tunisian Government. The 4-month mission has been formed in response to Tunisia's request to the Technical Cooperation Program of the International Cooperation Administration for expert assistance in modernizing her administrative structure and executive staffing.

The John Fleming Medal of the American Institute of Geonomy and Natural Resources was presented on 14 May to Dr. and Mrs. J. B. HERSEY at the Woods Hole Oceanographic Institution. The medal awarded was "for outstanding accomplishment in science and human welfare," on recommendation of the board of directors of the AIGNR and 67 foreign correspondents representing 26 countries. The citation for the medal was delivered by Columbus O'D. Iselin, director of the institution, who stated:

"I did not suspect how rapidly Dr. Hersey would build up geophysics at this laboratory. He has advanced the fundamental subjects of the geology and geophysics of the ocean basins, and certainly has observed the rule that some of us have to have a practical idea from time to time in order to obtain money allowing all of us to do some science. Not only has Dr. Hersey turned out many practical ideas but he has also done much more than his share of turning out basic science. He has a very large administrative load, he spends time giving the Navy sound advice and he has brought large sums of money to the Institution with which to do basic science."

ROBERT E. FAIRES of the Naval Research Laboratory, Washington, D.C., has been appointed head of the transducer branch, Sound Division.

HERMAN H. GOLDSTINE has joined the staff of the IBM Research Center at Yorktown, N.Y., as research adviser. Goldstine has been conducting research in pure and applied mathematics as a permanent member at the institute for Advanced Study at Princeton, N.J., for the past 12 years. He was d rector of the computing laboratory, a he collaborated with John Von N mann in the design and development the first computer there.

RAYMOND A. WHEELER, lieute ant general, U.S. Army, retired, who an engineer consultant to the Inter tional Bank for Reconstruction and D velopment, has received the George W Goethals Medal of the Society of Ame ican Military Engineers in recognition his "exemplary duty while serving as t United Nations Commander of Salva and Clearing Operations of the Su Canal." Other winners of the society awards are as follows:

DONALD A. RICE, chief of the gra ity and astronomy branch of the Geode Division, Coast and Geodetic Survey, re ceived the Colbert Medal for his "im portant contributions to the Departme of Defense in the fields of gravimetr and topographic-isostatic reductions the deflection of the vertical and gravity."

RICHARD A. LAUGHLIN, Com mander, Civil Engineer Corps, U.S Navy, received the Morecll Medal fo his "outstanding performance of duty a Director of the Logistics Planning Divi sion of the Bureau of Yards and Docks."

WILLIAM F. CASSIDY, brigadie general, Corps of Engineers, U.S. Army received the Wheeler Medal for his "out standing leadership in directing the flood fighting and disaster relief activities of the Corps during the floods of 1955–1956 in California."

EDWARD C. GILL, Colonel, U.S Air Force, received the Newman Meda for his "outstanding accomplishments in the administration of military engineering affairs for the Air Materiel Command and the United States Air Force."

JOHN W. N. SCHULZ, brigadier general, U.S. Army, retired, received the Gold Medal for Distinguished Service for his "unselfish devotion to the welfare of The Society."

At a dinner commemorating the 25th anniversary of the founding of the American Institute of Nutrition held during the annual meeting of the Federation of American Societies for Experimental Biology at Philadelphia, LEMUEL D. WRIGHT, professor of nutrition at Cornell University, was awarded the Borden Award in Nutrition, and PAUL GYÖRGY, professor of pediatrics and pediatrician-in-chief at the Hospital of the University of Pennsylvania, received the Osborne and Mendel Award. The Borden Award is given annually by the Borden Company Foundation, Inc., the Osborne and Mendel Award by the Nutrition Foundation, Inc.

György is internationally known for his contributions to basic nutrition. Milestones in his research career include the

...overy of riboflavin and of vitamin ... He recently reported the isolation and ...stallization of a new microbiological ...wth factor for the microorganism ...robacillus bifidus, which is found in ...man colostrum and human milk.

...MAX FINK, director of the depart...nt of experimental psychiatry at Hill... Hospital, Glen Oaks, N.Y., and ...STON HAVENS and co-workers of ... Massachusetts Mental Health Center, ...ston, Mass., were jointly awarded the ...r annual A. E. Bennet Psychiatric Re...rch Award by the Society of Biologi... Psychiatry at its 13th annual conven... in San Francisco on 11 May ...8.

...HOWARD J. ROGERS, a senior ...mber of the scientific staff of the ...dical Research Council, National In...ute for Medical Research, London, is ...iting professor at the LaRabida–Uni...sity of Chicago Institute, Chicago, Ill., ... the quarter ending 14 June. He has ...blished papers on aspects of the bio...ical synthesis of enzymes and muco...ysaccharides by bacteria, and on the ...chemistry of the mammalian skele...n.

...GORDON ALEXANDER, head of ... department of biology at the Uni...sity of Colorado since 1939, has re...ned from administrative duties, effec...e 1 July, to return to full-time teach... and research.

...C. GUY SUITS, president of the ...eneral Electric Research Laboratories, ...s been elected chairman of the Naval ...search Advisory Committee. He suc...eds FREDERICK E. TERMAN, dean ... the School of Engineering and director ... the Electronic Research Laboratory, ...anford University. FREDERICK ...ITZ, chairman of the department of ...ysics, at the University of Illinois, was ...ected vice-chairman. He assumes the ...ce-chairmanship previously held by ...uits. The committee is the Navy De...rtment's senior research advisory ...oup. It advises the Secretary of the ...avy, the Chief of Naval Operations, ...d the Chief of Naval Research with ...spect to research and its utilization by ...e Navy. The committee considers ques...ons of policy on Navy-wide scientific ...oblems.

...ROGER TORY PETERSON, natu...list, author of many books, and editor ... Houghton Mifflin Company's Peterson ...eld Guide Series, has been awarded ...e Geoffroy Saint Hilaire Golden Medal ... the Société Nationale d'Acclimata...n et de Protection de la Nature, for ...s "wonderful work in the field of sci...ce, education and nature conservation, ...pecially bird protection."

The following scientists were included among the ten civil servants named as the outstanding federal career people for 1958 by the National Civil Service League.

HUGH L. DRYDEN, director of the National Advisory Committee for Aeronautics, was cited as "an outstanding scientist administrator whose personal growth from laboratory assistant to director shows the possibilities of a Federal career."

JOHN M. IDE, technical director, Underwater Sound Laboratory, New London, Conn., Navy Department, was cited for "outstanding achievements in research, development, and organization."

RICHARD E. McARDLE, chief, U.S. Forest Service, department of agriculture, was cited for his work in conservation, achieved by "friendly and effective cooperation between industry, the States, and the Federal Government."

EDMUND R. McCLUSKEY, professor and head of the department of pediatrics, University of Pittsburgh, has been named vice chancellor of the schools of the health professions at the university, effective 1 July. He succeeds ROBERT A. MOORE, who resigned to become president of the Downstate Medical Center of the State University of New York.

RAE WHITNEY, assistant research professor in biology and director, Mammalian Genetics and Breeding Laboratory, Boston University, has joined Bio-Research Institute, Incorporated, and Bio-Research Consultants, Cambridge, Mass., as biologist and director of animal production.

BRUCE P. BOGERT of the Bell Telephone Laboratories at Murray Hill, N.J., has received the Biennial Award of the Acoustical Society of America for his "substantial" contributions to the science of acoustics.

S. J. FOLLEY, head of the physiology department of the National Institute for Research in Dairying, Reading, England, will be in the United States until 18 June.

Scientific visitors to North America from the United Kingdom include the following.

J. B. Brown, member of the Medical Research Council's Clinical Endocrinology Research Unit, Edinburgh, Scotland, is working with Gallagher at the Sloan-Kettering Institute in New York until the end of October.

G. J. GOODRICH, senior scientific officer of the National Physical Laboratory, Teddington, will be in the United States from 15 to 28 June to attend the Seminar on Ship Behavior at Sea to be held at the Stevens Institute of Technology, 16–20 June, and to visit the David Taylor Model Basin, Washington.

F. P. W. WINTERINGHAM, senior principal scientific officer of the Pest Infestation Laboratory, Slough, will be in the United States, Canada, and Panama from 7 to 29 June as scientific consultant to the World Health Organization. His itinerary includes New York; Boston; Medford, Mass.; London, Ont.; Urbana, Ill.; and Panama.

## Recent Deaths

MASASHI ENAMI, San Francisco, Calif.; 44; zoologist; professor at the University of Gunma, near Hiroshima, Japan; 23 May.

VLADIMIR A. GORDIEYEFF, Baltimore, Md.; 49; director of medical research at the Chemical Warfare Laboratories, Army Chemical Center, Md.; assistant professor at Clarkson College of Technology and research associate at Columbia University, 1948–51; 30 Apr.

KURT W. HAESELER, New York, N.Y.; 56; president of American Gas and Chemicals, Inc.; former instructor in chemistry at Columbia University, New York University, Hunter College, and Pratt Institute and associate professor of chemistry at Long Island University; 18 May.

JOHN K. HOSKINS, Chevy Chase, Md.; 74; former Assistant Surgeon General and, from 1943 until his retirement in 1948, chief of the Sanitary Engineering Division of the Public Health Service; 16 May.

HAROLD HOUSMAN, Pontiac, Mich.; 36; chief of psychology at the Pontiac State Hospital; former psychology instructor at the University of Michigan; 17 May.

STEPHEN S. HUDACK, Enumclaw, Wash.; 58; consultant in surgery of Community Memorial Hospital, Enumclaw; founder and director of the division of surgical research of Saint Luke's Hospital, Cleveland, 1952–57; author of many articles on medicine and surgery; 13 May.

ALBERT N. O'NEILL, Halifax, N.S., Canada; 38; associate research officer at the Atlantic Regional Laboratory of the National Research Council of Canada and leader of the section of organic chemistry since 1951; known for his investigations in carbohydrate chemistry; 7 May.

LEAH S. SHAFFER, New Orleans, La.; 53; research associate in the department of microbiology, Tulane University School of Medicine.

WILLIAM H. SHELLENBERGER, Westfield, N.J.; project engineer with the Esso Research and Engineering Company in Linden, N.J., for 25 years; 21 May.

# Book Reviews

**Sorok Let Sovetskovo Zdravookhraneniya, 1917–1957.** (Forty years of Soviet health protection). Ministry of Health Protection, U.S.S.R. Medgiz, Moscow, 1957. 662 pp. 26 rubles.

This large book, handsomely bound in red and gold, was issued by the Ministry of Health of the Soviet Union to celebrate the occasion of the 40th anniversary of the Communist regime in Russia.

The scope of the book is best indicated by the titles of the 23 chapters, as follows: "The protection of health in the USSR"; "History of the development of the Soviet health system"; "Sanitation and epidemiology"; "History of the development of urban medical services"; "Medical and sanitation services for industrial workers"; "The struggle against tuberculosis"; "The struggle against venereal and skin diseases"; "Oncologic services"; "Psychiatric services"; "Health on railroad transport"; "Medical and public health services for rural populations"; "The health of women and children"; "Health resorts, sanatoria and rest homes"; "Military medicine"; "Medical personnel, their education and training"; "Medical science"; "Medical press"; "Medical libraries"; "Medical industry"; "Pharmacy enterprises"; "Public health education and personal hygiene"; "The Society of the Red Cross and Red Crescent"; and "Professional association of medical workers."

Among the contributors are Maria Kovrigina, the present Minister of Health of the U.S.S.R., and her two predecessors, E. I. Smirnov, now Surgeon General of the armed forces, and G. A. Miterev, now head of the Red Cross and Red Crescent Society.

There are four full-page portraits—of Lenin, Semashko, Pavlov, and Burdenko. Pavlov remains the patron saint of Soviet medical science; Semashko was the first Commissar of Health and probably the most important single individual in the establishment of the Soviet system of public health; Burdenko was a neurosurgeon, a hero of the Soviet Union, and first president of the Academy of Medical Sciences. In keeping with the present fashion in Soviet history writing, more recently deceased or living political personages are not mentioned, and the chauvinism of the latter part of the Stalin period has been moderated.

Many of the chapters contain tables and figures demonstrating the growth and development of medical resources in the Soviet Union. The material is selected, of course, and the basic definitions often are somewhat different from those used in the United States. Conclusions and comparisons should be made, therefore, only after careful study and cross-checking of the data. In this regard, two recent books of information on Soviet health resources are particularly important. These are the fourth edition of K. V. Maistrakh's *Organizatsiya Zdravookhraneniya* (Organization of Health Protection) (Medgiz, Moscow, 1956) and the Ministry's *Zdravookhraneniye v SSSR. Statisticheskii Spravochnik* (Health Protection in USSR. Statistical Handbook) (Medgiz, Moscow, 1957).

The population of the Soviet Union was stated to be 200 million in 1956, of which 87 million were urban and 113 million were rural residents. These 200 million people were served by 329,000 physicians, or 16 per 10,000 population (although this figure includes some personnel that would not be classified as members of this profession in the United States). Soviet physicians were assisted by 930,000 feldshers, midwives, nurses, and other trained individuals and by over 1.5 million other workers in the field of health protection for a total complement of 2.78 million employees, or almost 3 percent of the civilian labor force. There were 1.36 million beds in 24,105 hospitals throughout the Soviet Union, or 67 beds per 10,000 population.

Distribution of physicians by the 15 republics comprising the Soviet Union varies from 10 per 10,000 population in the Tadzhik S.S.R. to 16 per 10,000 in the Russian S.F.S.R. The urban-rural differences, however, continue to be large. Thus, although 14,790 of the total 24,105 hospitals were rural, there were 313,170 beds in the rural hospitals, or 23 percent of the total number of beds in the U.S.S.R. Only 36,686 physicians, or 11 percent of the total for the country, were assigned to rural areas. Apparently a considerable proportion of the medical needs of the rural population was met by feldsher–midwife stations, of which there were 68,300, all in rural areas.

In 1956 the Soviet Union had 77 medical "higher educational institutions," which included 68 medical schools, two stomatologic institutes, and seven pharmaceutical institutes. This system had an enrollment of over 150,000 students and graduated 16,600.

The 1956 budget of the Ministry of Health was 34,600 million rubles. This represents approximately 3.5 percent of the gross national product and an annual per capita cost of approximately 170 rubles. This sum covered the salaries of 2.78 million employees, almost all therapeutic and preventive-medical services, sanitation, medical education, and medical research. Medical activities of the armed forces are budgeted separately.

By contrast with the exact figures given on the material resources, the data provided on the actual health conditions of the population continue to be disappointingly sparse. Kovrigina states (page 2[illegible]) that the crude death rate in the U.S.S.R. was 8.2 in 1955 and 7.7 in 1956 and that the life expectancy in 1955 was [illegible] years. The direct tabular comparison she makes with the United States and other countries is of quite limited meaning without information regarding the age and sex distribution, possible exclusion of certain groups, and other definitions of the population covered or information about the statistical methods by which these figures were derived.

Morbidity rates for seven major infectious diseases are tabulated (page 9[illegible]) but, unfortunately, these are restricted to comparative data for 1929 and 1[illegible]. The claims of virtual elimination of malaria and of typhus, as well as of the classical pestilential diseases, are not supported by actual rates or basic figures. In this same regard, although it is an interesting fact that 6,321,100 people received tuberculosis vaccinations in 1956 (page 164), the volume presents no concrete information regarding either morbidity or mortality from tuberculosis in the U.S.S.R. during the whole Soviet regime. Apparently, detailed health statistics still remain either unavailable or a state secret, and until these become available for analysis, many of the official statements must be considered to be unsupported. It is to be hoped that meaningful morbidity and mortality data from the Soviet Union may be supplied for the next anniversary volume.

The book is, of course, like most official summations of this kind, meant to portray the nation's health protection system in a favorable light; nevertheless it contains a wealth of information, and its omissions are also sometimes quite revealing. It is to be hoped that this book, as well as Maistrah's volume and the statistical handbook mentioned above, will be translated into English, in full, and widely distributed so that American physicians and health scientists can reach their own conclusions. The Soviet system of medicine, based on concepts so different from ours, is

working fact about which we should be thoroughly informed and which we should try to understand.

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**Graphic Methods in Structural Geology.** William L. Donn and John A. Shimer. Appleton-Century-Crofts, New York, 1958. viii + 180 pp. Illus. + plates. $4.

Thinking in terms of three dimensions is an essential skill for geologists, and graphic representation ranks with words and numbers as a means of transmitting geological thought. Therefore Donn and Shimer's subject is important. Their book is a convenient manual of those common graphic methods which should be mastered not only by students but by geologists engaged in practical work. The authors assume no previous experience and little knowledge on the part of the reader. They "lead the student by the hand" from extremely simple to more advanced material.

Although the emphasis of the book is upon graphic methods of solving problems, elementary means of geologic representation are also included. Geologic sections and block diagrams are introduced in a paragraph or two for beginners but are not fully discussed. Geologic maps are given more attention, particularly with respect to relations between structure, topography, and areal distribution patterns of rock units. This treatment could be readily understood by students who are just beginning structural geology, and some of it could be understood by liberal arts students or persevering laymen.

The greater part of the book is devoted to graphic methods of obtaining quantitative solutions to structural problems and is not intended to enthrall the nontechnical reader. Orthographic projection is completely described—from true and apparent dip to advanced fault problems in which inclined faults have oblique net slip. One of the ingredients of many solutions is the arbitrarily chosen structure contour, and the authors wisely introduce this conspicuously, early in the game.

Stereographic projection is explained briefly and well. The relative advantages of stereographic and orthographic methods are indicated. Stereographic solutions are developed for apparent dip, strike and dip from vertical drill-core data, intersecting surfaces, plunge, pitch, and certain fault displacements. In addition, there is an explanation of the procedure of rotating the sphere of projection about a horizontal or inclined axis to solve "two tilt" and other important problems which are almost uniquely amenable to stereographic treatment. The use of stereonets in structural petrology is not specifically described, but the basic principles are adequately covered.

The degree of accuracy of the presentation appears to be good, and only a few probable errors were noted. Several illustrations in the first 50 pages are rather crudely drawn, but the great majority of the 103 figures are clearly executed.

The authors and readers should be well satisfied with this book. It will be particularly useful to geology students who have not had courses in descriptive geometry and to those who wish to understand stereographic methods. Other, more complete, treatments are available, but many of these deal only with one segment of the subject matter which Donn and Shimer have compiled so compactly.

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**Physics.** Erich Hausmann and Edgar P. Slack. Van Nostrand, Princeton, N.J., ed. 4, 1957. x + 722 pp. Illus. $8.

**Fundamentals of Physics.** Henry Semat. Rinehart, New York, ed. 3, 1957. 914 pp. Illus. $8. (Also available in two vols.)

**Physics.** A textbook for colleges. Oscar M. Stewart. Sixth edition by Newell S. Gingrich. Ginn, Boston, ed. 6, 1957. viii + 756 pp. Illus. $6.50.

These three current revisions of well-known texts for a one-year course in college physics are evolutionary rather than revolutionary versions of earlier editions. In each there are refinements such as upgrading of the paper stock, re-drawing of figures with greater use of shading or perspective to make diagrams clearer, changes in the order of topics and chapters, and the omission or abbreviation of certain topics to make space for new material, with no significant change in overall length or character of the work.

All three continue to adhere to the classical division of physics into mechanics, heat, sound, electricity and magnetism, light, and atomic physics, and in essentially this order. *Hausmann-Slack* has 26 pages on radiation and atomic structure and 17 pages on solid-state electronics; *Semat* has 104 pages on atomics and nucleonics and about a page on transistors and semiconductors. *Stewart-Gingrich* has 25 pages on atomic physics and makes little mention of modern solid-state theory. An effort has been made in each book to solve the problems of units—a matter of great concern to many physics teachers. The trend from centimeter-gram-second units to meter-kilogram-second units is clear, but the transition is not complete. Particularly in electricity, it would seem better for both *Semat* and *Stewart-Gingrich* to work with only one (meter-kilogram-second) system of units.

*Hausmann-Slack,* clearly a text for engineering students or science majors, uses a considerable amount of mathematical background and some calculus. The discussions are brief and to the point, and satisfactorily rigorous. Perhaps the best feature of the new edition is the inclusion of new problems—problems which are varied, interesting, and challenging and which involve many up-to-the-minute situations. *Semat* uses no calculus, some trigonometry. It should be sufficiently rigorous and complete for students majoring in sciences but not too difficult for nonscience majors. The discussions are particularly clear and accurate, and the problems are varied and not too difficult. The discussion questions at the end of each chapter (they are not merely review questions) offer a particularly valuable supplement to the more usual problems. Probably all science courses should require students more frequently to analyze situations clearly and accurately in words and symbols, in addition to learning to solve problems for numerical answers. *Stewart-Gingrich* is designed for a general college physics course for students with no special mathematical background. It uses a rather standard, classical approach. While some sections are extremely well written, it tends more often than the other two books to give oversimplified, and occasionally inaccurate, statements and underived or unexplained formulas. Most chapters conclude with a brief, factual summary.

All three books have been used and liked by teachers for some years; the new editions will continue to serve in essentially the same types of courses and for the same types of teaching.

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**Biochemical Preparations.** vol. 5. David Shemin, Ed. Wiley, New York; Chapman and Hall, London, 1957. viii + 115 pp. $4.75.

*Biochemical Preparations* is designed to provide reliable procedures for the preparation of substances of biochemical interest and to illustrate valuable techniques and methods. It presents information about stability, properties, purification, and assay of the compounds included. This series may be warmly recommended to teachers, students, and research workers in biochemistry and related fields.

Two years have elapsed since the publication of the preceding volume. The editors hope subsequent issues may

appear regularly each year. They "more than welcome suggestions and the submission of well-described preparations of biochemical interest for future volumes."

In this volume carefully checked methods are presented for: the isolation of two enzymes, aldolase and crystalline condensing enzyme, and the purification of another, cytochrome *c*; the isolation of phosphatidyl ethanolamine, and of ribo- and 5′-deoxyribonucleotides, by ion exchange chromatography after alkaline and enzymatic hydrolysis, respectively, of the appropriate nucleic acids; the enzymatic preparations of nicotinamide mononucleotide and of S-adenosylmethionine; the chemical preparations of derivatives of biochemicals, sodium phosphocreatine, S-succinyl coenzyme A, L- and D-glutamine, and the formimino derivatives of glycine, L-aspartic acid and L-glutamic acid; the synthesis of adenine-8-$C^{14}$, dibenzyl phosphorochloridate, D-glyceric acid 2-phosphate, 2-deoxy-D-ribose, cyanomethylimidazole, imidazoleacetic acid hydrochloride, DL-, L-, and D-homocystine, DL-, L-, and D-homocysteine, and the S-benzyl derivatives of DL-, L-, and D-homocysteine.

A cumulative index of volumes 1 through 5 and a listing of the compounds of biochemical interest which have appeared in *Organic Syntheses* (through volume 37) are included.

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**Ion-Exchange Resins.** J. A. Kitchener. Methuen, London; Wiley, New York, 1957. vii + 109 pp. Illus. $2.

This small book appears at a time when interest in ion exchange is growing at a rapid pace. Chemists, biologists, and those in related fields seeking an introduction to the subject should find this book useful.

The organization is fairly standard. The first two-thirds of the book contain chapters on types of ion exchange materials, preparation of ion exchange resins, and the thermodynamics and kinetics of exchange processes. Discussion of chromatographic plate theory is brief but pertinent. In the last third of the book, some typical applications of synthetic ion exchangers, particularly to column separations of inorganic and organic substances, are described. Ion exchange membranes and their applications are discussed. The treatment of the various topics is necessarily brief, of course, in a book of this size, and readers already familiar with the field will not find the discussions as valuable as those found in more detailed books and review articles which have recently appeared.

The subject matter is presented in a clear and readable style. References to original literature are minimal, and those actually given should serve as an excellent starting point for a more detailed pursuit of the subject.

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**The New India.** Progress through democracy. Planning Commission, Government of India. Macmillan, New York, 1958. x + 412 pp. Illus. Cloth, $5; paper, $2.50.

This book is an abbreviated version of two recent official publications of the Government of India dealing with the achievements of the First Five Year Plan (1951–56) and the progress and objectives of the Second Five Year Plan, to be completed in 1961. It is written for the nonspecialist and is designed to give the general reader exhaustive information on what India has done, continues to do, and hopes to achieve in its efforts to improve its economic performance and the standard of living of its population. The book is written in a lively style, and since several Americans with long experience in India have collaborated with highly placed Indian officials in its composition, its contents not only have the ring of authenticity but also give due consideration to the interests of Westerners. The book is well illustrated, and some of the more important economic relationships are presented in well-designed tables. In addition, the main achievements and targets under the plans are summarized at the beginning of each chapter, under the general caption "highlights." Hence, by its presentation and its scope, the book forms an excellent introduction to the understanding of India and especially of India's efforts towards economic progress.

Since the book is put out by an official agency of the Indian Government its main strength consists in the facts and data it presents and not in the critical evaluation of these data. To be sure, the social and economic problems of India are well explained, but the solutions presented are only the official ones, and they are accepted without question as the best and most suitable. Thus, the picture that an ordinary reader without special firsthand knowledge about India gains is too rosy and too pat. The New India still has many facets of the Old India. In fact, India is a country in which practices and ways of acting characteristic of several different centuries coexist. There are religious practices which go back to the days of the Vedas, 3000 years ago. There are farming practices which have changed little in the last 2000 years. There are artisans who remind one of the craftsmen of the medieval world, and there are offices and shops which were up to date in the time of Queen Victoria. Next to them are buildings which foreshadow the 21st century, and factories and mills equipped with the most modern automatic machinery. In this book only these last are included in the New India, and very little is said about the tenacity and even the vigor of old institutions. This tenacity is bound up with the over-all cultural values of the Indian people, and in concentrating exclusively on the contents of the Five Year Plans and disregarding largely this cultural background, the book does not adequately convey a picture of all the forces at work in present-day India. Traditions of nonviolence, political factionalism, the caste system and its manifestations, and other forms of social behavior, many of which have deep roots in Indian life and culture, are either treated lightly or completely omitted. Yet the actual success of the plans—the meeting of the ambitious targets set out so clearly in the book—is contingent upon the changes which will occur in these cultural and social ways of behavior and not merely on the crores of rupees that will be spent on the manifold projects so clearly described in this work.

But apart from these shortcomings, which are due primarily to the official character of the work, this is an excellent, highly readable introduction to India's current economic problems and prospects.

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## New Books

*Loyalty and Security.* Employment tests in the United States. Ralph S. Brown, Jr. Yale Univ. Press, New Haven, Conn., 1958. 541 pp. $8.

*Le Volcanisme Lunaire et Terrestre.* Origine des continents, des océans et des atmosphères; l'énergie géothermique. Alexandre Dauviller. Michel, Paris, 1958. 300 pp. Paper, F. 1200.

*Nuclear Reactor Experiments.* Staff of Argonne National Laboratory. J. Barton Hoag, Ed. Van Nostrand, Princeton, N.J., 1958. 495 pp. $6.75.

*Standard Methods of Clinical Chemistry.* vol. II. American Assoc. of Clinical Chemists. David Seligson, Ed. Academic Press, New York, 1958. 229 pp. $5.50.

*A Comprehensive Dictionary of Psychological and Psychoanalytical Terms.* A guide to usage. Horace B. English and Ava Champney English. Longmans, Green, New York, 1958. 608 pp. $10.75.

*The Story of Archaeology.* Agnes Allen. Philosophical Library, New York, 1958. 245 pp. $4.75.

*Functional Bracing of the Upper Extremities.* Miles H. Anderson. Raymond B. Sollars, Ed. Thomas, Springfield, Ill., 1958. 478 pp. $9.50.

*Biology, a Basic Science.* Elwood D. Heiss and Richard H. Lape. Van Nostrand, Princeton, N.J., 1958. 659 pp. $4.88.

*College Physical Science.* Wendell H. Galbaugh and Alfred B. Butler. Prentice-Hall, Englewood Cliffs, N.J., 1958. 508 pp. $7.95.

*The Brain and Human Behavior.* Proceedings of the Association, 7–8 Dec. 1956. vol. XXXVI, Research Publ., Assoc. for Research in Nervous and Mental Disease. Williams & Wilkins, Baltimore, Md., 1958. 575 pp. $15.

*A Search for Man's Sanity.* The selected letters of Trigant Burrow, with biographical notes. Editorial Committee, Lifwynn Foundation. Oxford Univ. Press, New York, 1958. 639 pp. $8.75.

*Strategic Surrender.* The politics of victory and defeat. Paul Kecskemeti. Stanford Univ. Press, Stanford, Calif., 1958. 296 pp. $5.

*Physics Problems.* College Outline Series. Clarence E. Bennett. Barnes & Noble, New York, 1958. 255 pp. $1.75.

*Cloud Study.* A pictorial guide. F. H. Ludlam and R. S. Scorer. Macmillan, New York, 1958. 80 pp. $2.95.

*Analyzing Psychotherapy.* Solomon Katzenelbogen. Philosophical Library, New York, 1958. 126 pp. $3.

*Basic Mathematics.* H. S. Kaltenborn, Samuel A. Anderson, Helen H. Kaltenborn. Ronald, New York, 1958. 401 pp. $4.75.

*The Motility of Muscle and Cells.* Hans H. Weber. Harvard Univ. Press, Cambridge, Mass., 1958. 69 pp. $3.50.

*Pollen and Spore Morphology/Plant Taxonomy.* Gymnospermae, Pteridophyta, Bryophyta. G. Erdtman. Almquist & Wiksell, Stockholm; Ronald, New York, 1957. 151 pp. $8.

*Basic Principles of Chemistry.* J. Rae Schwenck and Raymond M. Martin. Prentice-Hall, Englewood Cliffs, N.J., 1958. 411 pp. $6.75.

*Nature Is Your Guide.* How to find your way on land and sea by observing nature. Harold Gatty. Dutton, New York, 1958. 287 pp. $4.95.

*Advances in Applied Mechanics.* vol. 5. H. L. Dryden and Th. von Karman, Eds. Academic Press, New York, 1958. 469 pp. $12.

*Graphic Methods in Structural Geology.* William L. Donn and John A. Shimer. Appleton-Century-Crofts, New York, 1958. 188 pp. $4.

*Principles of Research in Biology and Medicine.* Dwight J. Ingle. Lippincott, Philadelphia, Pa., 123 pp. $4.75.

*General Zoology.* Gairdner B. Moment. Houghton Mifflin, Boston, 1958. 644 pp. $7.50.

*The Mushroom Hunter's Field Guide.* Alexander H. Smith. Univ. of Michigan Press, Ann Arbor, 1958. 197 pp. $4.95.

*Ward 4.* The Mallinckrodt Research Ward of the Massachusetts General Hospital. James Howard Means. Harvard Univ. Press, Cambridge, Mass., 1958. 202 pp. $4.50.

*Principles of Electricity.* An intermediate text in electricity and magnetism. Leigh Page and Norman Ilsley Adams, Jr. Van Nostrand, Princeton, N.J., ed. 3, 1958. 545 pp. $7.50.

*The Pattern of Asia.* Norton Ginsburg, Ed. Prentice-Hall, Englewood Cliffs, N.J., 1958. 943 pp. $11.65.

*Principles of Physical Chemistry.* Samuel H. Maron and Carl F. Prutton. Macmillan, New York, ed. 3, 1958. 797 pp. $8.50.

*Quantitative Analysis.* Willis Conway Pierce and Donald Turner Sawyer. Wiley, New York, ed. 4, 1958. 510 pp. $5.75.

*The Strategy of Chemotherapy.* Eighth symposium of the Society for General Microbiology held at the Royal Institution, London, April 1958. Cambridge Univ. Press, London, 1958 (for the Soc. for General Microbiology). ix + 360 pp. $7.

*Contributions to Embryology.* vol. XXXVI, Nos. 242 to 251. Carnegie Institution of Washington, Washington, 1957. 210 pp. Paper, $13.75; cloth, $14.75.

*Laboratory Exercises in General Zoology.* Harvey I. Fisher and James B. Kitzmiller. Saunders, Philadelphia, Pa., 1958. 227 pp. $4.

*Proceedings of the Sixth International Conference on Spectroscopy.* Held at Amsterdam in May 1956. W. van Tongeren and F. Freese, Eds. Pergamon, New York and London, 1957. 672 pp. $25.

*Theoretical Astrophysics.* V. A. Ambartsumyan, Ed. Translated from the Russian by J. B. Sykes. Pergamon, New York and London, 1958. 660 pp. $22.50.

*Aliphatic Fluorine Compounds.* A. M. Lovelace, Douglas A. Rausch, William Postelnek. Reinhold, New York; Chapman & Hall, London, 1958. 380 pp. $12.50.

*Introduction to the Theory of Sets.* Joseph Breuer. Translated by Howard F. Fehr. Prentice-Hall, Englewood Cliffs, N.J., 1958. 116 pp. $4.25.

*Introduction to the Bacteria.* C. E. Clifton. McGraw-Hill, New York, ed. 2, 1958. 572 pp. $7.50.

*Anatomy of the Chordates.* Charles K. Weichert. McGraw-Hill, New York, ed. 2, 1958. 906 pp. $9.50.

*Polysaccharides in Biology.* Transactions of the Second Conference, 25–27 April 1956, Princeton, N.J. George F. Springer, Ed. Josiah Macy, Jr. Foundation, New York, 1958. 328 pp. $5.

*Methods of Biochemical Analysis.* vol. VI. David Glick, Ed. Interscience, New York, 1958. 367 pp. $8.50.

*Blacklock and Southwell, a Guide to Human Parasitology for Medical Practitioners.* Revised by T. H. Davey. Williams & Wilkins, Baltimore, Md., ed. 6, 1958. 230 pp.

*Handbook of Basic Microtechnique.* Peter Gray. McGraw-Hill, New York, ed. 2, 1958. 261 pp. $6.

*Qualitative Analysis.* An introduction to equilibrium and solution chemistry. Therald Moeller. McGraw-Hill, New York, 1958. 560 pp. $6.50.

*L'Enfant Neanderthalien du Pech de l'Aze.* Etienne Patte. Masson, Paris. 1957. 234 pp. Paper, F. 2500.

*Engineering Surveys: Elementary and Applied.* Harry Rubey, George Edward Lommel, Marion Wesley Todd. Macmillan, New York, ed. 2, 1958. 191 pp. $6.75.

*Physics of Nuclear Fission.* Supplement No. 1 of the Soviet Journal *Atomnaya Energiya.* Translated by J. E. S. Bradley. Pergamon, New York and London, 1958. 188 pp. $9.

*Timber Resources for America's Future.* Forest Resource Rept. No. 14. Forest Service, U.S. Dept. of Agriculture, Washington, D.C., 1958 (order from Supt. of Documents, GPO, Washington 25). 722 pp. $7.

*A Guide to Engineering Education.* Frank W. Eller. Teachers College, Columbia Univ., New York, 1958. 55 pp. $1.

*Nuclear Radiation Detection.* William J. Price. McGraw-Hill, New York, 1958. 389 pp. $9.

*Industrial Uses of Nitrogen in the United States.* Organisation for European Economic Co-operation, Paris, 1958. 132 pp. $3.

*College Mathematics.* Kaj L. Nielsen. Barnes & Noble, New York, 1958. 320 pp. $1.95.

*Function Fluctuation.* Monograph supplements, *Brit. J. Psychol.*, XXX. Charles C. Anderson. Cambridge Univ. Press, New York, 1958. 105 pp. $4.

*The Extra Pharmacopoeia.* vol. I. Pharmaceutical Press, London, ed. 24, 1958 (order from Rittenhouse Book Store, Philadelphia). 1725 pp. £3 5s.

*The Atomic Age and Our Biological Future.* H. V. Brøndsted. Translated by E. M. Huggard. Philosophical Library, New York, 1957. 94 pp. $2.75.

*Symposium on Latency and Masking in Viral and Rickettsial Infections.* The proceedings of a conference held at the University of Wisconsin Medical School, 4–6 Sept. 1957. Duard L. Walker, Robert P. Hanson, Alfred S. Evans. Burgess, Minneapolis, Minn., 1958. 211 pp. $4.75.

*The Problem of Scientific and Technical Manpower in Western Europe, Canada and the United States.* 2nd report. Organisation for European Economic Co-operation, Paris, 1958. 221 pp. $2.

*A Guide to Plastics.* C. A. Redfarn. Iliffe, London; Philosophical Library, New York, 1958. 160 pp. $7.50.

*Progress in Plastics 1957.* Papers and discussions at the British Plastics Convention 1957. Phillip Morgan, Ed. Iliffe, London; Philosophical Library, New York, 1958. 402 pp. $22.50.

*Analytical Mechanics for Engineers.* Fred B. Seely, Newton E. Ensign, Paul G. Jones. Wiley, New York; Chapman & Hall, London, ed. 5, 1958. 491 pp. $7.25.

*Progress in Stereochemistry.* vol. 2. W. Klyne and P. B. D. de la Mare, Eds. Academic Press, New York; Butterworths, London, 1958. 330 pp. $8.80.

*Our Nuclear Adventure.* Its possibilities and perils. D. G. Arnott. Philosophical Library, New York, 1958. 181 pp. $6.

*Modern Electroanalytical Methods.* Proceedings of the International Symposium on Modern Electrochemical Methods of Analysis, Paris, 1957. Sponsored by the I.U.P.A.C.'s Section on Analytical and Physical Chemistry. G. Charlot, Ed. Elsevier, Amsterdam, 1958. 195 pp. $4.95.

*Seals, Sea Lions, and Walruses.* A review of Pinnipedia. Victor B. Scheffer. Stanford Univ. Press, Stanford, Calif.; Oxford Univ. Press, London, 1958. 189 pp. $5.

# Reports

## Effect of a Pyridoxine Deficiency on Skin Grafts in the Rat

It has been amply demonstrated that the antibody response to a variety of antigens is markedly inhibited in a number of vitamin-deficiency states (*1*). The effect of a pyridoxine deficiency has been particularly well documented. In addition to induction by the usual dietary procedures, a pronounced deficiency of this vitamin can be rapidly induced by the administration of the antagonist, desoxypyridoxine. The latter experimental approach has been used to advantage in investigations on the role of pyridoxine in antibody production (*2*). It is generally accepted that the rejection of skin grafts from genetically dissimilar members within a given species (homografts) results from an immune response of the recipient to the antigens of the donor skin (*3*). The possibility was considered that this acquired immune response would be diminished in pyridoxine-deficient rats, with a resultant decrease in the magnitude of the rejection process. Thus, the study described in this report was undertaken to investigate the effects of a pyridoxine deficiency, induced in the rat by dietary means or by the administration of desoxypyridoxine, upon the rejection phenomenon of skin homografts.

Male, weanling rats of the Wistar and Long-Evans strains were purchased from commercial sources and were housed in individual cages. They were fed ad libitum a purified diet in which the B vitamins were furnished as a daily pill (*4*). Desoxypyridoxine, dissolved in isotonic sodium chloride, was administered daily by intraperitoneal injection. Pieces of skin of full thickness, measuring 2 by 2 cm, were excised from either the middorsum or the anterior abdominal wall of donor animals. All underlying fat and subcutaneous tissue were removed, and the skins were immediately applied to the host area to be grafted. The latter was prepared by removing a similar sized square of skin of full thickness from the middorsum, together with underlying fat and connective tissue, including the panniculus carnosus. Grafts were applied in reversed fashion so that hair growth was in the opposite direction to that of the host. No dressings were applied. Progress of the graft was followed closely by gross observation. Rejection was determined by ulceration, contraction, and final appearance of a fibrous scar. Histological examination supplemented the gross observations in doubtful cases. The absolute criterion of a successful graft ("take") included the absence of any of the above processes and the ultimate appearance of new hair growth in a direction opposite to that of the host. The success or failure of a graft could usually be assessed 3 weeks after the grafting procedure.

In the first series, comprising five separate experiments with a total of 400 rats, middorsal skin grafts were exchanged between (i) control, (ii) pyridoxine-deficient, and (iii) control and pyridoxine-deficient non-litter-mates of the Wistar strain after the animals had been maintained for 4 weeks on the experimental diets. Pyridoxine deficiency was produced by the omission of pyridoxine from the daily pill. Control rats received an identical diet supplemented daily with 50 μg of pyridoxine. Unless it is noted otherwise, the dietary regimen was not altered during the course of the experiment. Autografts of similar type were performed in both control and pyridoxine-deficient rats. The experimental period in this series varied from 3 to 10 weeks after the grafting procedure. During this time, many of the pyridoxine-deficient rats succumbed, while others, along with controls, were sacrificed. The results of these experiments are shown in Table 1. Grafts designated as "takes" at 3 weeks following grafting did not regress during the remainder of the experimental period. In three experiments involving 90 pyridoxine-deficient recipients (excluding autografts), 52 were alive 6 weeks after grafting. At this time, 80 percent of the grafts on these animals were considered "takes." In a separate experiment, seven pyridoxine-deficient recipients with successful grafts from pyridoxine-deficient donors were transferred to the control diet 4 to 8 weeks following grafting. All of these grafts were in excellent condition 24 weeks following their transplantation.

Table 1. Skin grafts in pyridoxine-deficient and control rats.

| Donor | Recipient: Strain | Recipient: Type | Total No. of rats | Percentage of "takes": 3–12 wk after operation | Percentage of "takes": 3 wk after operation | Percentage of "takes": 10 wk after operation |
|---|---|---|---|---|---|---|
| *Series 1 (dietary-induced deficiency)* | | | | | | |
| Control | | Control | 78 | 15 | | |
| Deficient | | Control | 67 | 28 | | |
| Control | | Deficient | 60 | 62 | | |
| Deficient | | Deficient | 62 | 90 | | |
| Autografts | | | | | | |
| Deficient | | | 64 | 86 | | |
| Control | | | 69 | 45 | | |
| *Series 2 (desoxypyridoxine-induced deficiency)* | | | | | | |
| | Long-Evans | Control | 71 | | 9 | 1 |
| | Long-Evans | Deficient | 50 | | 92 | 60* |
| | Long-Evans | Control† | 16 | | 0 | 0 |
| | Wistar | Control | 70 | | 4 | 1 |
| | Wistar | Deficient | 43 | | 63 | 2 |
| | Wistar | Control† | 16 | | 0 | 0 |
| Autografts‡ | | | | | | |
| | Long-Evans | Control | 24 | | 100 | |
| | Long-Evans | Deficient | 14 | | 86 | |
| | Wistar | Control | 23 | | 100 | |
| | Wistar | Deficient | 9 | | 100 | |

* Seventeen animals in this group have been observed for 18 to 21 weeks. Of these, five still have successful grafts.
† This group was treated exactly like the corresponding deficient group except that 1 mg of pyridoxine was given daily by intraperitoneal injection during the period of desoxypyridoxine treatment. The Long-Evans rats were fed the control diet immediately following cessation of desoxypyridoxine administration. No symptoms of pyridoxine deficiency were noted in these animals.
‡ Thirty of these autografts have been under observation for 10 to 18 weeks following grafting. All are in excellent condition. Autografts successful at 3 weeks following operation have never been noted to regress.

All technical papers are published in this section. Manuscripts should be typed double-spaced and be submitted in duplicate. In length, they should be limited to the equivalent of 1200 words; this includes the space occupied by illustrative or tabular material, references and notes, and the author(s)' name(s) and affiliation(s). Illustrative material should be limited to one table *or* one figure. All explanatory notes, including acknowledgments and authorization for publication, and literature references are to be numbered consecutively, keyed into the text proper, and placed at the end of the article under the heading "References and Notes." For fuller details see "Suggestions to Contributors" in *Science* 125, 16 (4 Jan. 1957).

The number of "takes" observed in control recipients indicates a certain genetic similarity between members of the Wistar strain employed (Table 1). However, it is apparent that resistance to skin grafts is markedly diminished in pyridoxine-deficient recipients. The use of donor skin from pyridoxine-deficient animals results in a greater percentage of successful grafts than does that of donor skin from controls in corresponding groups of recipients (*5*).

In the second series, consisting of three separate experiments with a total of 336 rats, skin grafts were exchanged between members of the Wistar and Long-Evans strains after the animals had been maintained for 3 weeks on the control diet furnishing 10 μg of pyridoxine daily. The rats grew well on this regimen and did not manifest any of the symptoms characteristic of a pyridoxine deficiency. Donor skin was taken from the anterior abdominal wall and grafted to the back. Autografts were performed on both Wistar and Long-Evans rats. Immediately following the grafting procedures, each strain was divided into two groups. One continued to receive the control diet for 5 to 6 weeks. Thereafter, survivors in this group were fed a commercial stock ration (Purina chow). Another group received the pyridoxine-free diet and was treated with desoxypyridoxine. Animals of the Long-Evans strain were given daily injections of 250 or 500 μg of desoxypyridoxine for 10 days and were continued on the pyridoxine-deficient diet for an additional 5 to 8 days. The Wistar rats were given similar daily injections of desoxypyridoxine during this period of 15 to 18 days. Typical symptoms of pyridoxine deficiency were evidenced in all desoxypyridoxine-treated rats. These pyridoxine-deficient animals were then fed the control diet for 3 to 5 weeks and the Purina chow ration for the remainder of the experiment. Results obtained with both levels of desoxypyridoxine were similar and are summarized together in Table 1.

As in series 1, the skin grafts in pyridoxine-deficient recipients of series 2 were far more successful than those in control recipients. In contrast to series 1, many successful grafts in series 2 were subsequently rejected. This was particularly true for the pyridoxine-deficient Wistar rats, in whom the incidence of rejection following an initial "take" at 3 weeks was exceedingly high. It should be noted that, at 3 weeks, the grafts of the pyridoxine-deficient Long-Evans rats were superior to those of the corresponding Wistar group. In further comparison with series 1, the absence of any mortality, the lesser incidence of "takes" in control homografts, and the higher incidence of "takes" in control autografts in series 2 are noteworthy. This last observation illustrates the superiority of full-thickness abdominal skin over full-thickness dorsal skin as donor material.

In summary, the survival time of skin homografts is increased markedly in pyridoxine-deficient rats. Some grafts are still in excellent condition 5 to 6 months following grafting. It is possible that this effect may be related to an inhibition of the immune response to the antigens of the donor skin in this deficiency state. The specificity of this effect and its mechanism are under study (*6*).

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6. This investigation was supported by grants from the National Vitamin Foundation, Inc., New York, the United Fund of Allegheny County, Pa., and the Division of Research Grants (No. RG 4624), National Institutes of Health, U.S. Public Health Service.

29 January 1958

## Influence of L-Ascorbic Acid on the Colchicine Reaction

Because of its relative specificity of cytological effect, the colchicine reaction should provide valuable information regarding the mechanism of mitosis (*1*). That the reaction has not done so to date is apparently due to the lack of knowledge concerning its mode of action in the cell (*2, 3*). One obvious approach to this problem is the careful study of substances which either suppress or enhance the reaction. Many such substances are known, but the majority are either moderately good antimitotic agents in themselves or must be used at very high dose levels (*2*).

Ascorbic acid has been reported to inhibit partially the effect of colchicine on tissue cultures of rabbit fibroblasts (*4*). Since L-ascorbic acid is a normal metabolite, reinvestigation of the reported antagonism of this substance on the colchicine reaction appeared to be worth while (*5*). To do this, use was made of the Bowen-Wilson *Pisum* test (*6*). This test consists essentially of treating standard size (2.5 to 3.5 cm) primary roots of young pea seedlings under standard conditions and examining their meristems for quantitative cytological changes in terms of frequency of diagnostic chromosome configurations relative to dose-time changes. Colchicine activity was measured by means of the colchicine index which was devised and studied for validity in our laboratory (*7*). This index is based on assigning values to specific chromosome configurations according to the severity of the colchicine effect represented by such configurations. Previous studies have shown that such an index changes smoothly with time and that the rate of change is dependent on dose. A given index at a given time represents a specific colchicine potency. Modification of the colchicine reaction may therefore be measured by differences between control and treatment indices at given times.

Table 1 summarizes our findings. Essentially, it was noted that treatment of colchicine for several hours with ascorbic acid at *p*H 7, followed by adjustment of the *p*H of the mixture back to 5.5 immediately prior to use, resulted in a lower index than that obtained in the colchicine control. While ascorbic acid has only a slight but measurable effect when it is used at one-half the molarity of the colchicine, it does have a much greater effect when its molarity is equal to that of colchicine ($1.25 \times 10^{-4}$). At twice the molarity of colchicine, ascorbic acid produced no significant change in effect over that produced by the equimolar concentration. A mixture of colchicine and ascorbic acid in a molarity

Table 1. Effects of L-ascorbic acid on the colchicine reaction.

| Test No. | Colchicine mol. ($\times 10^{-4}$) | Ascorbic acid. mol. ($\times 10^{-4}$) | *p*H | | Colchicine equivalent (%) | Enhancement in time |
|---|---|---|---|---|---|---|
| | | | Initial | Treatment | | |
| 1 | 1.25 | | 5.5 | 5.5 | 100 | 0 |
| 2 | 1.25 | 0.63 | 7.0 | 5.5 | 94 | −30 |
| 3 | 1.25 | 1.25 | 7.0 | 5.5 | 84 | −69 |
| 4 | 1.25 | 2.5 | 7.0 | 5.5 | 88 | −54 |
| 5 | 1.25 | 2.5 | 6.0 | 5.5 | 94 | −32 |
| 6 | 1.25 | 0.63 | 5.5 | 5.5 | 100 | + 2 |
| 7 | 1.25 | 1.25 | 5.5 | 5.5 | 101.5 | +22 |
| 8 | 1.25 | 2.5 | 5.5 | 5.5 | 102 | +36 |
| 9* | 1.25 | 2.5 | 5.5 | 5.5 | 102 | +30 |

* Roots were pretreated with ascorbic acid for 1 hour and then treated with colchicine.

ratio of 1:2 made up at *p*H 6, stored for several hours, and then adjusted to 5.5 just before it was used had a small but measurable suppressing effect (about equal to the 1:½ mixture at *p*H 7).

Obviously both the molarity of the ascorbic acid and the *p*H of the mixture are important factors. The latter is borne out by the fact that treatment of root tips with mixtures of colchicine and ascorbic acid at *p*H 5.5 produces an enhancement of the colchicine effect, the degree of which is dependent on the molarity of the ascorbic acid. Interestingly enough, pretreatment of root tips with ascorbic acid at two times the molarity of colchicine had virtually the same effect as combining the two compounds at *p*H 5.5 before use. While the latter might be considered to be an in vitro effect, the former must be an in vivo one.

Obviously, before a compound is designated as an enhancer or antagonist, the conditions of treatment must be stated. L-Ascorbic acid falls into both categories, depending, in part at least, on *p*H. However, alkaline *p*H's which produce rapid hydrolysis of the lactone ring (*8*) render the ascorbic acid ineffective. The effect of L-ascorbic acid on the colchicine reaction is determined by three factors (i) the *p*H, (ii) the relative molarity, and (iii) the integrity of the ascorbic acid molecule. Exactly how these factors are related mathematically remains to be determined.

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18 December 1957

## Reaction of Epinephrine with Ethylenediamine

The condensation of epinephrine with ethylenediamine (EDA) to form a fluorescent product was first reported by Natelson, Lugovoy, and Pincus (*1*). Weil-Malherbe and Bone (*2*) adapted this reaction to the fluorimetric quantitation of epinephrine and norepinephrine in blood.

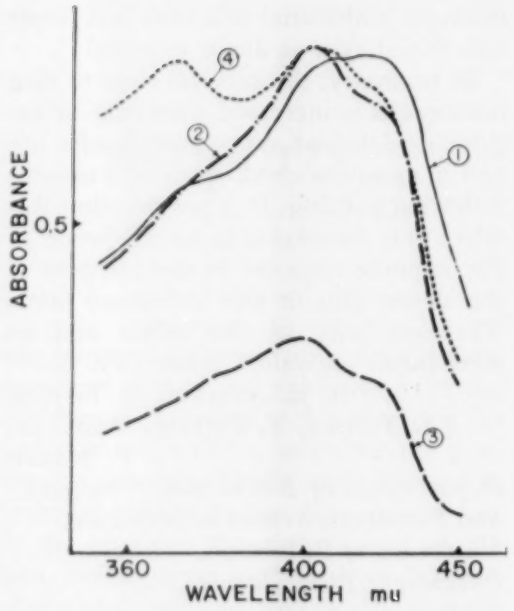


Fig. 1. Absorption spectra of fluorescent derivatives in isobutanol. Curve 1 is the product from 0.8 μM epinephrine, $1 \times 10^{-2}$ mole EDA, $1 \times 10^{-3}$ mole EDA dihydrochloride; curve 2 is the product from 0.8 μM epinephrine, $1 \times 10^{-3}$ mole EDA, $1 \times 10^{-4}$ mole EDA dihydrochloride; curve 3 is the product from 0.8 μM epinephrine, $1 \times 10^{-4}$ mole EDA, $1 \times 10^{-5}$ mole EDA dihydrochloride; curve 4 is the product from 0.8 μM epinephrine, $1 \times 10^{-2}$ mole EDA, $1 \times 10^{-3}$ mole EDA dihydrochloride, heated at 70°. Spectra were obtained using a Beckman DK-2 recording spectrophotometer.

While considerable attention has been given to improving the method of Weil-Malherbe and Bone, little work has been reported on the mechanism of this reaction and the nature of the products formed. Burn and Field (*3*) reported the formation of two fluorescent derivatives from norepinephrine by heating at 50° to 70°C with 5 percent EDA for 1.5 to 2 hours at *p*H 11. They obtained two fluorescent derivatives from epinephrine under similar conditions.

A study of the reaction of various catechols with EDA is underway in our laboratory. As part of this study, the reaction of epinephrine with EDA was carried out under various conditions of temperature, *p*H, and EDA concentration, and the products were examined by spectrophotometric and chromatographic techniques. The absorption spectrum of the products obtained under the conditions established by Weil-Malherbe and Bone (*2*) is represented by curve 1 of Fig. 1. The peaks at 400 and 415 mμ and the shoulder at 370 mμ each represent a different fluorescent derivative as shown by chromatographic separation on filter paper (*4*) and by spectrophotometric measurement of the eluted products. The compound with $\lambda_{max.}$ 370 mμ had an $R_f$ value of 0.22 and fluoresced blue-white; that with $\lambda_{max.}$ 400 mμ, $R_f$ 0.35, fluoresced blue-green; and the derivative with $\lambda_{max.}$ 4[illegible] mμ, $R_f$ 0.49, fluoresced yellow.

Changes in EDA concentration affected the relative proportion of the fluorescent derivatives formed in this reaction. A stepwise reduction of the EDA concentration resulted in a gradual increase in the ratio of the absorbance at 400 mμ to that at 415 mμ. Curve 2 of Fig. 1 represents the effect of a tenfold decrease in EDA concentration. A 100-fold decrease in EDA concentration resulted in lesser amounts of all three derivatives (curve 3, Fig. 1). The higher EDA concentration (curve 1, Fig. [illegible] gave a *p*H of 10.6. All other concentrations were adjusted to this *p*H with saturated trisodium phosphate solution.

The effect of increased temperature is illustrated by curve 4 in Fig. 1. At 70°C a significantly greater amount of derivative with $\lambda_{max.}$ 370 mμ was formed. Heating for longer than 20 minutes at 50°, 70°, or 100°C decreased the yield of all three derivatives.

Maximum amounts of the blue-green and yellow fluorescent compounds were formed at *p*H 10.6, lower yields being obtained at *p*H 9.5 or 11.0.

Weil-Malherbe and Bone furnished evidence that adrenochrome is an intermediate in this reaction (*2*). This fact has been verified in the present study. Adrenochrome and epinephrine yielded identical products with EDA as demonstrated by absorption spectra and paper chromatography.

Bubbling oxygen through the reaction mixtures increased only slightly the yields of fluorescent material. In fact, substitution of adrenochrome for epinephrine, in which case oxygen is not required (*2*), does not increase the yields of fluorescent compounds. This is contrary to the results of Burn and Field (*3*) who reported that the oxygen dissolved in the solution was not sufficient for maximum yields of fluorescent material.

Norepinephrine, in contrast to epinephrine, formed only two fluorescent derivatives under the same conditions, one having $R_f$ 0.33 fluoresced blue-green, the other, $R_f$ 0.49, fluoresced yellow (*4*). The spectrum of this fluorescent material was similar to that reported by Burn and Field (*3*), which showed a single peak at 420 mμ in isobutanol. The difference in the reaction of epinephrine and norepinephrine with EDA cannot be explained at this time (*5*).

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23 December 1957

## Plaque Morphology and Pathogenicity of Vesicular Exanthema Virus

Two recent reports have described a correlation of plaque-type mutants of polioviruses with reduced virulence for monkeys and mice, respectively (*1*). However, variation of plaque morphology with antigenic type has not been described. This report describes intertype variations in plaque morphology among seven types of vesicular exanthema of swine virus, as well as intratype variations which have been correlated with differences in virulence for the natural host.

Plaque formation is obtained by infecting monolayers of a transmissible swine kidney cell, PK-2a (*2*), by means of the prescription bottle method of assay (*3*). The nutrient agar is similar to that described by Youngner (*4*). After incubation of infected cultures at 36° or 37°C, plaques can be seen as early as 24 hours. These continue to increase in size and number for 7 to 10 days, although 90 to 95 percent of the plaque count is obtained within 96 hours. Marked variation in plaque morphology is observed not only between virus types but also within virus types. Characteristic plaques of two of the seven virus types are shown in Fig. 1. With the exception of the $G_{55}$ virus, two types of plaques are seen: a large, clear, round plaque which appears after 24 to 48 hours' incubation and increases in diameter to 5 to 8 mm within 96 hours, and a minute, opaque plaque, frequently irregular in shape, usually not visible until 72 to 96 hours have passed, which rarely exceeds 1.5 mm in diameter, even with 7 to 10 days' incubation. Pronounced differences in the ratio of the number of minute and large plaques, as well as in the size of plaques, are found between virus types. Some of the plaque characteristics observed are listed in Table 1.

The theoretical possibility that the large or minute plaques might be produced by a contaminating virus was excluded by the following series of experiments with $E_{54}$ type virus. Stocks of "pure" large plaque formers (Lpf) and minute plaque formers (Mpf) of E type virus were prepared after three successive plaque purifications. The stocks could be considered pure only in a relative sense. As yet there is no suitable selective technique by which a small number of large plaque formers can be detected in the presence of a large number of minute plaque formers, and vice versa. Thus, viral suspensions which contained 1 large plaque former among 1000 minute plaque formers or 1 minute plaque former among 1000 large plaque formers were considered 99.9 percent pure. To determine whether both plaque variants were capable of producing vesicular exanthema, groups of swine were inoculated intradermally on the lip with $10^7$ plaque-forming units of wild type (mixed) $E_{54}$ virus, plaque purified E (Lpf) and purified E (Mpf). The ratios of minute plaque formers to large plaque formers in these three inocula were approximately 50:1, 0.001:1; and 1000:1, respectively. Temperatures were taken daily, and the presence or absence of primary and secondary vesicles was noted over an 18-day period. When possible, fresh vesicle coverings were obtained to determine the plaque type of the recovered virus. Two weeks after inoculation all animals were bled to obtain convalescent serum for neutralization tests.

Inoculation of the wild type virus and of the large plaque formers produced typical vesicular exanthema in four out of four animals, especially severe in the case of the latter. Four animals which received $10^7$ plaque-forming units of minute plaque formers (which may have contained as many as $10^4$ large plaque formers) exhibited no elevation of temperature over a 7-day period after infection, but each developed a single small lesion at the site of inoculation on the 6th or 7th day. No secondary lesions were observed. The absence of a febrile reaction prior to vesicle formation, the mildness of the primary lesions, and the absence of secondary vesicles constitute a picture of extreme atypical vesicular exanthema. These results indicate that the large plaque former is highly virulent for swine and that the minute plaque former either is essentially avirulent or is greatly reduced in pathogenicity.

Suspensions were made of vesicle coverings from infected swine and tested for

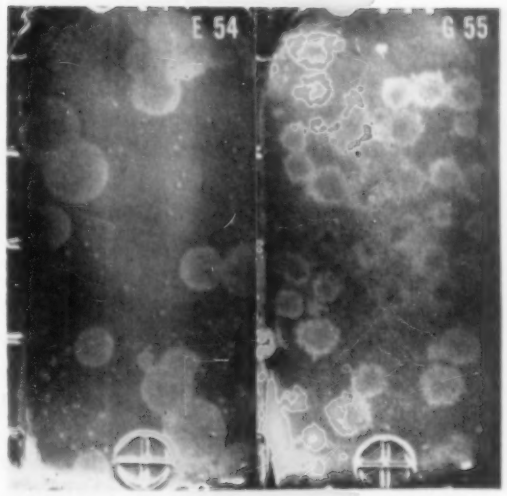


Fig. 1. Plaque morphology of vesicular exanthema of swine virus, types $E_{54}$ and $G_{55}$, on transmissible swine kidney monolayers.

plaque type of the recovered virus. Only the large plaque former was recovered, even from animals infected with the minute plaque former. This result substantiates the hypothesis that the large plaque former is the virulent virus particle and suggests that the mild disease produced in the swine inoculated with the minute plaque former was actually caused by the 0.1 percent of the large plaque former in the inoculum.

Cross-neutralization tests carried out by plaque assay method demonstrated the antigenic identity of the large plaque former and the minute plaque former. Convalescent sera from the three groups of infected swine were diluted 1 to 50, mixed with an equal volume of diluent containing about $10^8$ plaque-forming units of either wild type $E_{54}$ virus, E (Lpf) or E (Mpf), held 1 hour at room temperature, and assayed for residual infective virus. Serum from each group of infected swine neutralized 90 to 95 percent of the plaque-forming activity of all of the three virus suspensions, indicating close immunological relationship.

There appears to be no published report of the occurrence of such extreme differences in plaque morphology among different antigenic types of a single virus

Table 1. Characteristics of plaque variants of vesicular exanthema of swine virus on transmissible swine kidney cells.

| Virus | Plaque size at 96 hr (mm) | | Hour when 90% plaque count was obtained | No. of minute plaques per large plaque |
|---|---|---|---|---|
| | Large | Minute | | |
| | | *Group I* | | |
| $A_{48}$ | 5–10 | 1 | 72 | 2 |
| $D_{53}$ | 5–8 | 1 | 72 | 10 |
| $E_{54}$ | 5–10 | 0.5 | 96 | 100 |
| $G_{55}$ | 5–7 | | 72 | $< 0.001$ |
| | | *Group II* | | |
| $B_{51}$ | 2–3 | 1 | 96 | 100 |
| $C_{52}$ | 2–4 | 1 | 96 | 100 |
| $F_{56}$ | 2–3 | 0.5 | 72 | 1–3 |

as those observed with vesicular exanthema of swine virus. Were the correlation only between plaque morphology and type, it would be interesting but not particularly meaningful in a biological sense. However, the fact that differences in plaque morphology of a virus were correlated with extremes of pathogenicity in a natural host lends more than academic interest to the observations. The findings with polio viruses previously mentioned and those with the virus described in this report (*5*) suggest that the correlation of physiological and morphological plaque variations with host pathogenicity may reflect a phenomenon common to other species.

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27 January 1958

## Absence of Albuminlike Serum Proteins in Turtles

The differentiation of species of turtles of the genus *Pseudemys* by paper electrophoresis of serum proteins was reported recently (*1*). However, no turtle serum proteins comparable in electrophoretic behavior to human serum albumin were observed. Other workers (*2*) have reported marked differences between the electrophoretic patterns of turtles and snakes. A biochemical comparison of the total protein and albumin content of reptilian sera (*3*) revealed notably lower albumin values in turtles than in snakes. However, the particular salting out procedure of that study did not exclude alpha globulins from the albumin fraction.

During our studies (*4*) with serum proteins of human beings and lower vertebrates with neoplasia, paper electrophoresis techniques did not reveal albuminlike components in sera of normal representatives of three major families of turtles. Turtle families and species studied were Chelydridae (*Chelydra serpentina*), Dermochelidae (*Dermochelys coriacea*), and Testudinidae (*Clemmys insculpta* and *Testudo gigantea*).

Sera were collected from clotted samples of blood obtained by cardiac puncture. Our paper electrophoresis was done with a Spinco apparatus, at 5 ma constant current for 16 hours. Paper strips were stained with bromphenol blue and were photoscanned and analyzed by means of the Spinco-Analytrol instrument. Specimens of human serum were included in each run. Rat and alligator serum proteins were compared with those of a turtle by a biuret procedure following a modified salt-ether fractionation (*5*) of the blood sera.

The turtle sera examined appear free of a human-like albumin serum protein component, according to electrophoretic analyses (Fig. 1). Ether-salt fractionation and biuret analysis did not consistently reveal albuminlike protein in the serum of *Chelydra* (Table 1).

The findings are provocative from the viewpoints of comparative biochemistry, physiology, and systematics. Albumin synthesis is a function that has long been ascribed to the parenchymal cells of the liver (*6*). Such cells are reported to be structurally cirrhotic-like in the liver of fish, amphibians, and reptiles (*7*). Interestingly enough, paper electrophoresis of the blood serum of Elasmobranchii (*8*) has revealed no component with the mobility of albumin. Correlations between liver histology and protein biochemistry are not available for reptiles. Such studies might be of phylogenetic value. Boyden and Paulsen (*9*) have emphasized the value of electrophoretic studies of serum proteins as a step toward understanding the biochemical evolution of the vertebrates. However, physical chemical criteria, in addition to paper electrophoresis, and protein analyses of greater sensitivity than the biuret reaction are necessary before one can satisfactorily define the nature of the presence or absence of "albumin" in the sera of turtles or other lower vertebrates.

The results reported here suggest an absence of a human-like serum protein with electrophoretic properties of albumin in more than one genus and family of turtles. Similar independent observations of Zweig and Crenshaw (*1*) are supported by our work.

Table 1. Rat, alligator, and turtle serum proteins (grams per 100 ml of serum). For this study, serum of one male specimen of Holtzman albino rat and of one male specimen of *Alligator mississipiensis* and pooled sera of three specimens of *Chelydra serpentina* were used. The "albumin" fraction from the serum of another specimen of *Chelydra* did give a faint biuret reaction.

| Protein | Rat (g/100 ml) | Alligator (g/100 ml) | Turtle (g/100 ml) |
|---|---|---|---|
| Total protein | 5.95 | 5.80 | 2.20 |
| Albumin plus alpha globulins | 3.12 | 1.80 | 2.03 |
| Albumin | 2.14 | 0.70 | 0.00 |
| Alpha globulins | 0.98 | 1.10 | 2.03 |
| Other globulins | 2.83 | 4.00 | 0.17 |

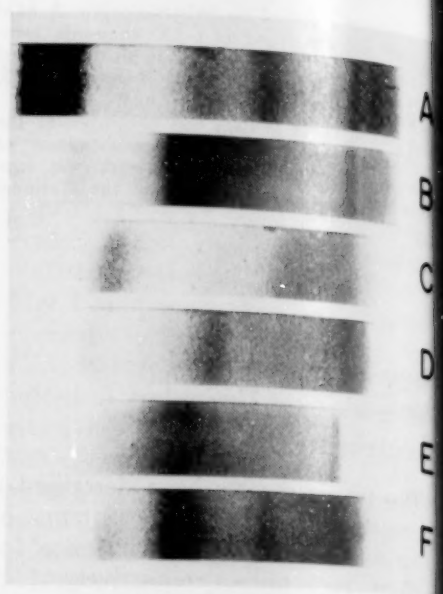


Fig. 1. Paper electrophoresis patterns of serum proteins of turtles and of the serum proteins of a human being (*A*) and an alligator (*B*) for comparison. Other patterns represent the turtle species *Dermochelys coriacea* (*C*), *Clemmys insculpta* (*D*), *Testudo gigantea* (*E*), and *Chelydra serpentina* (*F*).

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13 December 1957

## Inhibition of Ribonuclease by Polyacids

Heparin and other sulfated polysaccharides have been reported to act as competitive inhibitors of beef pancreas and rodent liver ribonucleases (*1*, *2*). Two well-recognized effects of heparin have been reproduced with the polyacids

icotungstic, phosphotungstic, and phosomolybdic. These are (i) anticoagut activity in vitro and in vivo (*3*); ) the ability to elicit the appearance plasma clearing factor activity (*3*). he work discussed in this report demstrates that these inorganic substances so resemble heparin in their ability to hibit crystalline beef pancreas ribonuease. In addition, dextran sulfate (*4*) d two sulfated pectic acid derivatives hich possess anticoagulant activity (*5*) re also found to be potent ribonucle- inhibitors.

Ribonuclease activity was determined the spectrophotometric method of unitz (*6*) at *p*H 5.0. Each of the subances was brought to *p*H 5.0 before ddition to the test system. The polyids were commercial products.

The data given in Table 1 demonrate that all five of the polyacidic subances inhibit ribonuclease activity unr these conditions. Relative inhibitory tivity seems to fall in the general der: dextran sulfate > sulfated pectic id amide > sulfated pectic acid methyl ster > silicotungstate > phosphomolybte. In general, the sulfated polysacarides were more active than the inganic polyacids.

Since pepsin has the lowest isoelectric oint of any known protein (*7*), a samle was inactivated by alkali treatment ), then adjusted to *p*H 5.0. This maial showed very little ribonuclease inibitory activity. This result is in marked ntrast to the inhibition obtained by andendriessche (*2*) with polyaspartic id and indicates that proper spacing of the polyacidic groups is also an important characteristic of this type of ribonuclease inhibitor (*9*).

Table 1. Inhibition of ribonuclease (RNase) by polyacids.

| Amt. added (mg/4 ml) | RNA added (mg/4 ml) | Decrease in $A_{300}$ between 1 and 5 min. after mixing | Relative RNase activity (%) |
|---|---|---|---|
| | *Silicotungstate* | | |
| None | 0.9 | 0.038 | 100 |
| 0.20 | 0.9 | 0.002 | 5 |
| 0.10 | 0.9 | 0.008 | 21 |
| 0.08 | 0.9 | 0.014 | 37 |
| 0.06 | 0.9 | 0.021 | 55 |
| 0.04 | 0.9 | 0.034 | 89 |
| 0.02 | 0.9 | 0.035 | 92 |
| | *Phosphomolybdate* | | |
| None | 0.9 | 0.035 | 100 |
| 0.6 | 0.9 | 0.035 | 100 |
| 0.8 | 0.9 | 0.023 | 66 |
| 0.8 | 1.2 | 0.034 | 97 |
| | *Dextran sulfate* | | |
| 0.2 | 0.9 | 0.001 | 3 |
| 0.1 | 0.9 | 0.004 | 11 |
| 0.02 | 0.9 | 0.012 | 34 |
| | *Sulfated pectic acid methyl ester* | | |
| None | 1.2 | 0.036 | 100 |
| 0.10 | 1.2 | 0.012 | 34 |
| 0.05 | 1.2 | 0.025 | 71 |
| | *Sulfated pectic acid amide* | | |
| 0.05 | 1.2 | 0.020 | 57 |
| | *Inactivated pepsin* | | |
| None | 1.2 | 0.042 | 100 |
| (1.0) | 1.2 | 0.038 | 90 |



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9. This research was supported in part by a grant from the National Institutes of Health, U.S. Public Health Service (A803).

31 December 1957

## Antihypertensive Effects of an Aldosterone Antagonist

A new synthetic steroid was recently described (*1*) that antagonized the renal excretory effects of aldosterone and deoxycorticosterone acetate (DCA) in rats (*2*) and man (*3*): 3-(3-oxo-17β-hydroxy-4-androsten-17α-yl)propionic acid γ-lactone (SC-5233). It was of interest to examine the ability of this compound to prevent and reverse the experimental hypertension produced in rats by DCA.

In the first experiment, two groups of eight 1-month-old Sprague-Dawley rats were implanted with a 20-mg DCA pellet and offered 0.86-percent NaCl as drinking fluid. In addition, one group received SC-5233, 10 mg/kg per day subcutaneously for 19 days, and the other group received the solvent (propylene glycol). Blood pressures (*4*) were taken periodically under standard "double-blind" conditions. No differences between the blood pressures of the two groups were observed after 1, 5, or 10 days of treatment. However, on the 15th and 18th days, the mean pressure of the treated group was 168 mm, while that of the untreated group was 177 and 181; these differences were significant (*5*) at the 5- and 1-percent levels, respectively. Because of these results, investigations are under way to determine whether SC-5233 will prevent the production of adrenal-regeneration hypertension (*6*), which may involve hyperreactivity to aldosterone (*7*).

Additional experiments were performed on metacorticoid hypertensive rats (*8*), which are no longer under the active metabolic influence of DCA (*9*). This form of experimental hypertension resembles essential hypertension in man, particularly with regard to the pharmacology, physiology, and pathology of the two diseases (*10*).

For acute studies, SC-5233 was injected into 12 metacorticoid rats, and the blood pressures were recorded before and 2, 4, and 6 hours after injection. Twelve hypertensive control rats received the solvent. It was found that the compound had a hypotensive action when it was administered by both the oral and parenteral routes (Table 1).

For chronic studies, two groups of six metacorticoid rats drinking saline were observed for 7 days and then injected with SC-5233 or the solvent for 19 days. The total dose of SC-5233 over this period was 800 mg/kg (subcutaneously). Blood pressures were recorded five times during the pretreatment week, 14 times during treatment, and twice after; SC-5233 caused a significant decrease of pressure, which was reversed after the cessation of therapy (Table 2). This experiment was subsequently repeated at a dosage of 280 mg/kg in 14 days, with the same results.

The ability of SC-5233 to block the pressor action of DCA is consistent with its ability to block the renal excretory actions of DCA and aldosterone (*2*, *3*). However, its hypotensive action in metacorticoid hypertensive rats can hardly be due to the same process, since such rats are no longer being subjected to DCA overdosage (*9*). Additional evidence is provided by the finding that we have been unable to uncover any activity of the 19-nor derivative of SC-5233 in blocking the pressor action of DCA in saline-fed rats or in lowering the blood pressure of metacorticoid hypertensive rats, in spite of the fact that this deriva-

Table 1. Acute hypotensive action of SC-5233 in metacorticoid rats.

| Time of treatment | Blood pressure (mm) | |
|---|---|---|
| | SC-5233 | Controls |
| *Experiment A** | | |
| Before injection | 190 | 190 |
| 2 hr after injection | 169† | 194 |
| 4 hr after injection | 170† | 192 |
| 6 hr after injection | 166† | 193 |
| *Experiment B‡* | | |
| Before injection | 188 | 188 |
| 2 hr after injection | 166§ | 194 |
| 4 hr after injection | 162§ | 192 |
| 6 hr after injection | 160§ | 194 |

* A, 20 mg/kg subcutaneously (eight rats per group).
† $P < 0.01$ that change in pressure equals that of controls (*5*).
‡ B, 200 mg/kg by gavage (four rats per group).
§ $P < 0.05$ that change in pressure equals that of controls (*5*).

Table 2. Chronic hypotensive action of SC-5233 in metacorticoid rats; SC-5233 was administered on days 8 to 27, inclusive.

| Day | Blood pressure (mm) | |
|---|---|---|
| | SC-5233 | Controls |
| 1–7 | 184–208 | 182–210 |
| 9 | 176* | 189 |
| 11 | 169† | 190 |
| 15 | 162† | 191 |
| 17 | 158† | 181 |
| 21 | 153† | 179 |
| 23 | 157* | 177 |
| 25 | 155† | 180 |
| 28 | 160* | 177 |
| 32 | 174 | 183 |

* $P < 0.05$ that change of pressure equals that of controls (5).
† $P < 0.01$ that change of pressure equals that of controls (5).

tive is considerably more potent than SC-5233 in blocking the renal excretory effects of DCA (2). Apparently the renal mineralocorticoid-blocking and the antihypertensive properties of SC-5233 are not directly related. Instead, the latter property might be mediated by the reversal of some internal electrolyte disturbance that had been instituted by the temporary treatment with DCA, such as an increase in the intracellular sodium compartment (11–13).

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12. A detailed report by C. M. Kagawa *et al.*, on the pharmacology of SC-5233 is in preparation.
13. The technical assistance of Esther Lacunza and Gladys Powers is gratefully acknowledged.

13 March 1958

## Lack of Competitive Inhibition between Beef and Monkey Growth Hormones in Rhesus Monkeys

The demonstration that growth hormone obtained from monkey pituitary glands is physiologically effective in the rhesus monkey while that from beef glands is not (1, 2) led to the finding of distinct physicochemical differences between the molecules of the two growth hormones (3). These results suggested the possibility that beef growth hormone, which is inactive in the monkey, might mask the effects of monkey growth hormone on nitrogen retention by competing for "effector sites" when the two molecules are administered concurrently to hypophysectomized rhesus monkeys.

Two immature male monkeys (*Macaca mulatta*) which had been hypophysectomized approximately 1 year before were placed on a nitrogen balance regimen, as previously described (2). Following a control period, each animal received daily intramuscular injections of monkey pituitary growth hormone (prepared by A. E. Wilhelmi) at a dosage of 1 mg/kg; one animal was treated for 7 days, the other for 9 days. This was followed by a 10-day control period. On the following day each monkey received an intramuscular injection of 10 mg of beef growth hormone (4) per kilogram. In the succeeding week each animal was given daily intramuscular injections of beef growth hormone (10 mg/kg) and monkey growth hormone (1 mg/kg). Daily nitrogen balance determinations were made throughout the control and experimental periods. The mean daily nitrogen retention and its standard error were calculated for each period.

The results obtained for each of the hypophysectomized monkeys were essentially the same and are illustrated in Fig. 1 with data from one of them. The anabolic effect of the monkey growth hormone preparation was not significantly reduced by the concurrent administration of beef growth hormone in a ratio of 10:1 by weight.

In both experiments a slight tendency toward a reduction in nitrogen retention when both hormones were administered was noted. This reduction, however, was not stastistically significant. It would seem from the foregoing data that the specificity of the "effector sites" for growth hormone action in the monkey is such that beef growth hormone, in relatively large quantities, although physiologically inert in this species, does not mask the action of the monkey growth hormone molecule. These "effector sites" in the rat do not exhibit such specificity, since in this animal monkey and beef growth hormones are equally effective (2, 5).

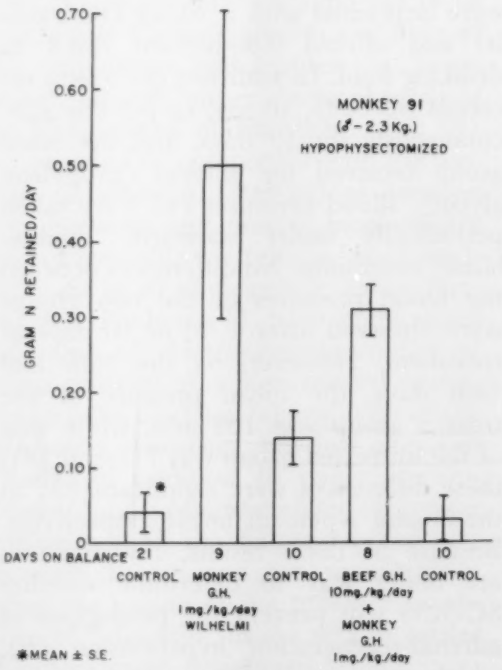


Fig. 1. Effect of concurrent administration of beef and monkey growth hormones on nitrogen retention in a hypophysectomized rhesus monkey.

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5. We wish to express our gratitude to Dr. D. McGinty of Parke, Davis & Co., Dr. Mary Root of Eli Lilly & Co., Dr. Joseph Seifter of Wyeth, Inc., Dr. R. H. Barnes of the Sharp & Dohme Division of Merck & Co., Inc., and Dr. C. A. Bunde of Pittman-Moore & Co. for generous gifts of monkey pituitary glands. The beef growth hormone (Somar-A) was a gift of the Endocrinology Study Section of the National Institutes of Health. The technical assistance of John Cimerol is gratefully acknowledged. This study was supported by a grant from the American Cancer Society (EDC-1) and a grant from the National Institute of Arthritis and Metabolic Diseases (A-292), National Institutes of Health, U.S. Public Health Service.

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3 February 1958

## Microbiological Fractionation of the Hydrogen Isotopes

Mass spectrometric analyses of bacterially generated gas made in early 1957 as an adjunct to U.S. Geological Survey studies of Bahama Banks sediments unexpectedly revealed a high concentration of light hydrogen (protium), presumably with segregation elsewhere of the heavy isotope deuterium. Further investigation is intended, but meanwhile it seems advisable to record our findings to date in sufficient detail to provide a point of departure for others who may be interested (1).

As a part of a comprehensive plan for study of Bahamas sediments collected by

loud and associates in May 1955, bac-riological analyses of the refriger-ed samples were undertaken by Sisler, ginning early in 1956. It was soon ob-rved that a yet unidentified (2) facul-ive aerobe found in teeming abun-nce in aragonite muds from a mid-nk locality west of Andros Island (Fig. station G4) produced gas vigorously en it was cultured in a dextrose me-um (3). It seemed likely that this gas s largely $CO_2$, but a check-analysis s sought from the Mass Spectrometry ction of the National Bureau of Stand-ds. That analysis, by Dibeler, showed 3 percent carbon dioxide and 63.4 rcent hydrogen; the latter, within the solving power of the apparatus, ap-ared to consist exclusively of common ht hydrogen. The balance was 5.3 per-nt water vapor, 4.6 percent nitrogen, d 0.4 percent oxygen.

There is, of course, nothing unusual out the concentration of hydrogen by cteria (4). The striking aspect of ibeler's analysis was its indication that e hydrogen was markedly enriched in e light isotope. The apparent magni-de of the enrichment was so unexpected at an independent analysis of a new s sample from the same bacterial cul-re was run by Friedman, on a newly stalled Geological Survey mass spec-ometer especially designed for study of e hydrogen isotopes. Friedman's re-lts showed that the deuterium was de-eted by a factor of 20 over ocean water, ther than by the factor of 3.7 to be ex-ected from evaporation and the equilib-um

$$H_2O + HD \rightleftharpoons H_2 + HDO$$

This situation was so remarkable that ydrogen isotope analyses were later run y Friedman) on the water of inclusion d the whole dextrose from the same tch that was used in preparation of the lture medium, as well as on a sample the dextrose formula actually used to epare the station G4 gas sample, in-uding the mixture of lower Chesapeake y water and distilled water employed roughout the tests. Since these three sts all showed normal isotopic abun-nce, it is certain that the fractionation served is performed by the bacteria emselves.

Meanwhile, an opportunity had arisen return to the Bahamas in June 1956, d further work on the hydrogen was

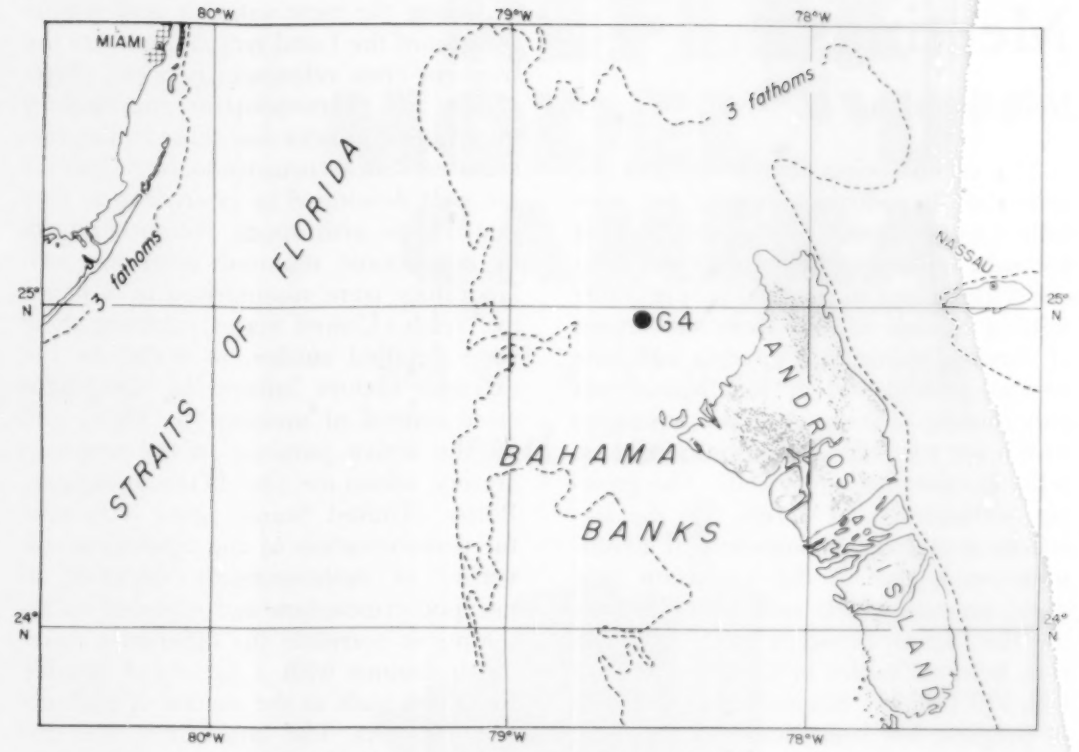


Fig. 1. Index map showing location of station G4.

deferred pending field observations to determine whether the gas was generated (and fractionated) in place. At the approximate site of station G4 a trap was set to catch any gases moving upward from the sediment into the overlying water. No free gas accumulated in this trap over a 24-hour period, and accidental tipping of the trap prevented analysis of the enclosed water for dissolved gases. Further investigation was not practicable.

Regardless of what may happen in nature, however, it is certain that there exist, in at least one site in the calcium carbonate muds west of Andros Island, bacteria that, under appropriate circumstances, can vigorously produce hydrogen gas depleted in deuterium. An estimate of abundance by the minimum dilution technique indicates this bacterium to be present in the top 6 in. of sediment from station G4 in excess of $10^{10}$ units per gram wet weight. This unprecedented abundance might be in part due to bacterial increase during the year in which the sample was refrigerated before study, but control counts of the total number of bacteria in fresh muds indicate that allowance for such increase would not reduce the estimated exponent by more than 2 or 3 at most.

Inasmuch as the gas is depleted in deuterium, the deuterium is presumably concentrated within the interstitial water, the residual nutrients, or the bacteria. Such concentration of the normally scarce heavy isotope, if it should prove feasible to produce it in large-scale viable culture, suggests means to facilitate and reduce the cost of production of heavy water (5).

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### References and Notes

1. Publication of this report has been authorized by the director, U.S. Geological Survey, and the director, National Bureau of Standards.
2. Studies are under way to characterize and identify this bacterium, tentatively referred by Sisler to the genus *Pseudomonas*.
3. Composition of the medium was as follows: Bacto-dextrose, 4.0 g; $(NH_4)_2HPO_4$, 0.2 g; $MgSO_4 \cdot 7H_2O$, 0.2 g; $FeCl_3$, 0.2 g; normal sea water, 750 ml; distilled water, 250 ml.
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29 April 1958

# Meetings

## Neurosecretion

The view is being abandoned that the activities of endocrine organs are controlled by hormonal feedback only, as it becomes increasingly clear that the nervous system plays an essential part in transmitting stimuli to and from the organs of internal secretion. To this end, the nervous system has at its disposal not only nervous pathways but also hormones which are produced by specialized nerve cells, the neurosecretory cells. The growing realization that herein lies the significance of the phenomenon of neurosecretion is one of the important new developments which took place following the first Symposium on Neurosecretion, held at Naples in 1953 [see *Science* **118**, 579 (1953)]. Since then a good deal of progress has been made in this field with respect to the chemistry and electron microscopy of neurosecretory material; also, new sites of neurosecretory activity and new hormones produced by neurosecretory cells have been discovered in recent years. Another meeting of investigators active in this special area was proposed, therefore, by Bertil Hanström; it took place 1–6 July 1957, at the University of Lund (Sweden).

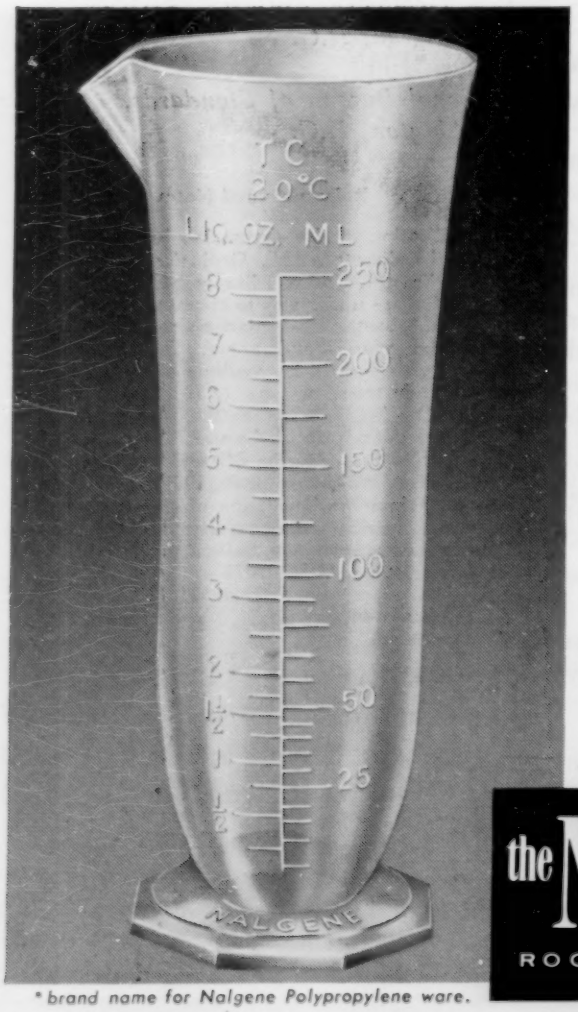
Among the most valuable and unique features of the Lund symposium were the frequent cross references between observations on neuroendocrine mechanisms in the invertebrates and those in the vertebrates. Such neuroendocrine systems are well developed in invertebrates, particularly in arthropods. Recent findings in crustaceans reported from his own laboratory were summarized in a paper by Welsh (United States). Among these were detailed studies, in crabs, on the external factors influencing the endocrine control of molting (by Bliss) and on the active particles in the neurosecretory substance (by Pérez-González). Potter (United States) gave a beautiful demonstration of the cytological diversity of neurosecretory material in decapod crustaceans and reported on attempts to correlate the differently staining inclusions with a variety of specific functions, such as the control of pigmentary effectors. The latter topic was discussed in greater detail by Kleinholz (United States).

In insects, the neuroendocrine pathways controlling postembryonic development and reproduction were analyzed by B. Scharrer (United States), who also read a paper by Nayar (India) on one such system in the insect *Iphita*. Possompès (France) discussed interesting relationships between the brain and the composite "ring gland" in the highly s cialized fly *Calliphora* and reported work by Dupont-Raabe (France) c cerning new types of neurosecret pathways in phasmids. These contri tions, as well as one by Johansson (N way) on neurosecretory phenomena *Oncopeltus*, led to fruitful discussi of the neuroendocrine pathways, o which, for example, malnutrition affe the endocrine control of the gonads invertebrates and vertebrates, includi man. The paper by Suomalainen (Fi land) reporting on the effect of the str of hibernation on the neurosecretory a tivity of the hypothalamic cells in t hedgehog was a further contribution this topic.

Investigations of this kind point t way for studies concerned with the cli ical aspects of neuroendocrinology. T contributions to the symposium by neur pathologists such as Lundberg (Sweden and Christ (Germany) were therefore much interest. Their data were compl mented by a variety of comparative hi tological observations by Sano (Japan and Legait (France). Present knowled on the electron microscopic character tics of neurosecretory elements was co firmed and extended by Bargmann (Ge many), Welsh (United States), an Knowles (Great Britain). In this rang of magnification the agreement betwe invertebrate and vertebrate data is pa ticularly impressive. The further explo ation of neurosecretory phenomena b means of the electron microscope, combination with phase contrast, da field, and fluorescence microscopy, pro ises many interesting insights. Other ne techniques were employed by Malandr (Italy) and Sloper (Great Britain), wh studied the hypothalamo-hypophysial sy tem by using radioactive tracer element by Carlisle (Great Britain), who co firmed earlier observations by Potter an Lowenstein (1955) that neurosecreto axons are capable of conducting ele trical impulses; and by Mazzi (Italy) who tested the developmental potenci of the different parts of the amphibia hypophysis in relation to the hypo thalamus.

Some problems debated by investig tors, among whom were Sloper (Gre Britain), Schiebler (Germany), an Eichner (Germany), concerning the sol bility, staining properties, and topochem istry of neurosecretory substances we answered conclusively from the point view of the biochemist. According t Acher (France), the neurosecretory m terial consists of an "inactive" large pr tein molecule (neurophysine) and sever polypeptides with hormonal activitie Among the latter the most thorough known are the oxytocin and vasopress of the mammalian neurohypophysis. comparable chemical composition m also exist in invertebrates. Chromatopho


**NALGE** *Pharmaceutical Graduates*

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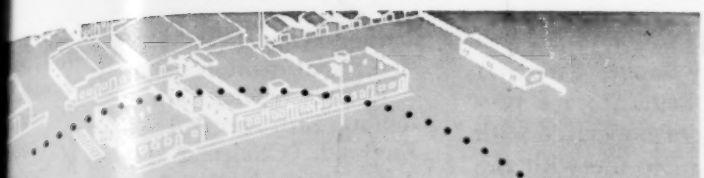

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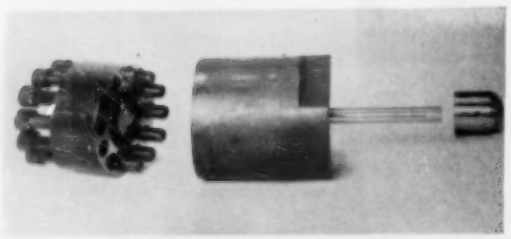

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otropins, for example, obtained in highly purified form by Fänge (Sweden) and Knowles (Great Britain), are presumed to be polypeptides associated with an "inactive" protein molecule with the same staining properties as those of the neurophysine of the vertebrates. Additional contributions concerning the chemical characterization of neurosecretory material in invertebrates were those by Rehm, reported by Welsh (United States), and by L'Hélias (France).

The question remains to be solved whether vasopressin is the mediator which releases corticotropin, as proposed by Martini (Italy), or whether this task is performed by a third polypeptide, chemically similar to vasopressin and oxytocin, as demonstrated by Saffran (Canada). Oxytocin may play an important role in the release of luteotropic hormone (prolactin) in the rat, as was pointed out by Stutinsky (France). The distribution of substance P in the central nervous system of fishes and its possible relationship to neurosecretory phenomena were discussed by Ostlund (Sweden).

The number of formal presentations was wisely reduced to five short papers per day. This left ample time for another important part of the symposium—namely, the exhaustive discussion of the problems posed by the lecturers. It should be mentioned, therefore, that a number of participants, while not presenting formal papers, made valuable contributions by their often extended remarks during the discussion. Among these, Wigglesworth (Great Britain), M. and E. Thomsen (Denmark), Karlson (Germany), and Rothballer (United States) might be especially mentioned.

The Lund symposium supplemented the exceedingly interesting eighth symposium of the Colston Research Society, held at Bristol in 1956 [see *Science* **126**, 456 (1957)], which was restricted to the neurohypophysis and did not concern itself with histochemical and electron microscopic studies. By necessity, it gave little attention to neurohormones other than vasopressin and oxytocin.

The Lund symposium again demonstrated the magnitude of the area in which neurosecretory phenomena of great diversity play important roles in neuroendocrine integration.


ERNST SCHARRER
BERTA SCHARRER

*Department of Anatomy, Albert Einstein College of Medicine, New York*


## Forthcoming Events

### July

*9–15.* Zoological Nomenclature Colloquium, London, England. (F. Hemming, 28 Park Village East Regent's Park, London, N.W.1.)

*10–14.* Research Methods in Soil Zoology, colloquium, Harpenden, Hertfordshire, England. (P. W. Murphy, Rothamsted Experimental Station, Harpenden.)

*12–14.* Biological Sciences, international union, 13th general assembly, London, England. (Chairman, Div. of Biology and Agriculture, National Research Council, Washington 25.)

*15–19.* Condensation Nuclei, 3rd intern. symp., Cambridge, England. (T. Wormell, Cavendish Laboratory, Cambridge Univ., Cambridge.)

*15–19.* Food Additives, 4th intern. symp., Paris, France. (M. E. Gradnauer, Documentation Center, Commission Internationale des Industries Agricoles, 6 avenue de Villars, Paris 7e.)

*15–22.* Association Française pour l'Avancement des Sciences, 77th congress, Namur, Belgium. (AFAS, 28, rue Serpente, Paris VIe, France.)

*15–23.* Educational Treatment of Deafness, intern. cong., Manchester, England. (A. W. G. Ewing, Dept. of Education of the Deaf, Univ. of Manchester, Manchester 13.)

*16–23.* Zoology, 15th intern. cong., London, England. (H. R. Hewer, c/o British Museum of Natural History, Cromwell Road, London, S.W.7.)

*20–27.* Americanists, 33rd intern. cong., San Jose, Costa Rica. (33rd intern. Cong. of Americanists, National Museum, P.O. Box 749, San Jose de Costa Rica, Central America.)

*21-24.* High Polymer Conf., intern., Nottingham, England. (Conference Secretariat, Dept. of Scientific and Industrial Research, Charles House, 5–11 Regent St., London, S.W.1.)

*21–25.* Diabetes, 3rd intern. cong., Düsseldorf, Germany. (K. Jahnke, Oberarzt, 2 Medizinische Klinik, Medizinische Akademie, Düsseldorf.)

*22–26.* Brazilian Soc. for the Progress of Science, 10th annual, São Paulo, Brazil. (Sociedade Brasileira para o Progresso da Ciencia, Caixa Postal 2926, São Paulo.)

*23–28.* Continuous Cultivation of Microorganisms Symp. (by invitation), Prague, Czechoslovakia. (I. Malek, Inst. of Biology, Czechoslovak Akad. of Sciences, Narodni Tr. 5, Prague I.)

*24–25.* Computers and Data Processing, 5th annual symp., Denver, Colo. (Electronics Div., Denver Research Inst., Univ. of Denver, Denver 10.)

*25–29.* Chromatic Discrimination in Animals and Man, ICSU symp., Paris, France. (H. Pieron, Collège de France, Place Marcelin-Berthelot, Paris 5e.)

*28–30.* Regulation of Cell Metabolism, Ciba Foundation symp. (by invitation), London, England. (G. E. W. Wolstenholme, 41 Portland Pl., London, W.1.)

*28–2.* Home Economics, 9th intern. cong., College Park, Md. (Congress Director, American Home Economics Assoc., 1600 20 St., NW, Washington 9.)

*28–8.* Statistical Summer Seminar, Dedham, Mass. (I. Weiss, Bell Telephone Labs., North Andover, Mass.)

### August

*4–9.* Microbiology, 7th intern. cong., Stockholm, Sweden. (F. C. Harwood, Soc. of American Bacteriologists, c/o Waverly Press, Inc., Mt. Royal and Guilford Aves., Baltimore 2, Md.)


*(See issue of 16 May for comprehensive list.)*

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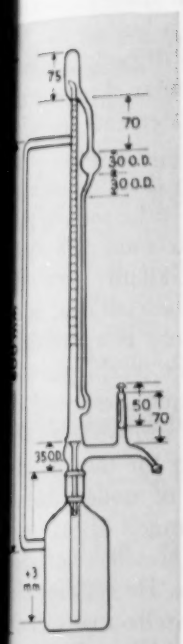


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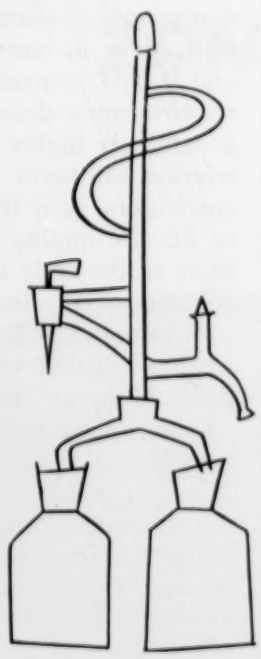

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# Letters

## Ammi majus

In the article "Effects of 8-methoxypsoralen and ultraviolet light in human skin" [*Science* **127**, 878 (1958)], the author, S. W. Becker, Jr., clearly demonstrated the mechanism of 8-methoxypsoralen action. However, I would like to point out that extracts of *Ammi majus* (Linné) have not been "used by the Egyptians . . . for centuries." In fact, the first extracts were made at Cairo University in 1954 [see I. R. Fahmy, A. A. Rahman, R. E. Hakim, *Proc. Pharm. Soc. Egypt Sci. Ed.* **38**, 67 (1956)].

Only the cremocarps (tiny fruits) of *Ammi majus* have been dispensed, by the nomadic Berberian tribe of Beni-Shoeïb, dwelling in the North African desert, who furnished them powdered in order to disguise the origin of the drug, which was called in Berberian "Atrillal" or the "bird's foot," due to the shape of the umbel that carries the cremocarps.

As reported by Ibn El Bitar (13th century), the secret was finally disclosed, and El Sherif (sixth century) was the first physician to administer these powdered cremocarps for leucoderma in a rather rational way. Dawood El Antaki (17th century), El Rashidi (19th century), and Maimonides all wrote extensively on this drug and its administration, but nowhere is there any mention of "extract" of the plant or its cremocarps.

RAOUF E. HAKIM
*M. D. Anderson Hospital, Houston, Texas*

Raouf Hakim's statements are correct. My choice of the term *extract* was a poor one; I meant crude preparations of the *Ammi majus plant*. The first true extracts were those prepared at Cairo University in 1954.

S. W. BECKER, JR.
*Whiting Clinic, Whiting, Indiana*

## Science Education

*Science* [**127**, 852 (1958)] reported the very important recommendations of the 1958 Parliament of Science. All scientists will recognize that several widely diverse aspects of our total educational problem were well discussed and helpfully reported by these meetings sponsored by the AAAS.

May one reader note, however, the existence of evidence in support of the view that those recommendations nevertheless essentially fail to come to grips with one problem which some observers now consider the central and most urgent of all our educational problems? I refer to the hardest of all tasks—getting more and


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better courses in the sciences and mathematics into the high-school curriculum and getting quickly a markedly higher percentage of the high-school population enrolled in all of these subjects. If, in high school, the necessary years are added to study of these subjects, those years will also be subtracted from some other exercise of study. The report is therefore quite unrealistic in the oft-repeated thought illustrated by the statement, "We believe that scientific education is best fostered as a part of a general emphasis on intellectual activity and that the pressing need is for increased support of the social sciences and humanities [foreign languages are elsewhere added] as well as the natural sciences." This approach stymies almost all efforts to bring about quantitative change.

Other sources have placed "the pressing need" elsewhere. The Report of the President's Committee on Scientists and Engineers (1 Dec. 1957) said: "There is ample evidence that the Soviet Union is bending every effort to achieve its goal of world domination by leading the way in this scientific revolution. . . . Russian advances in other technological fields present an equally grave threat to the ultimate security and wellbeing of our people." And Khrushchev confirmed t in March 1958 by stating that the Sov expect to win their contest with the W through education, industrial product and other nonmilitary means. The Pr dent's committee also clearly noted th to oppose the Russian threat, the co mittee's "educational program is larg directed towards the secondary scho . . . and [is designed] to persuade a hig proportion of the youngsters with scie aptitudes to choose science or engine ing as a career."

During the years 1936–45 I was cha man of a committee that gathered exte sive information on the status of biolo as a high-school subject and the pro lems that arise from inclusion of biolo in the curriculum and also obtained som insight on the status of chemistry an physics in the same 3100 high schools 48 states. For none of these sciences w the picture obtained a healthy one. A the inherent, built-in difficulties in ma ing the marked curricular changes clea demanded in the statements quoted the preceding paragraph seem to be si gularly overlooked in the Parliament r port. Neglected, too, is the warning giv in the documented account of a schol in literature, Joseph Gallant [*Science* 12 787 (1957)], who showed that, at th high-school level, there is a vast diffe ence between what the teaching of soci studies and the humanities could an ought to accomplish and what is *usual* done in high schools for the enlighte ment and motivation of modern studen He well shows that much of that teac ing is damagingly "prescientific" and denigration of science. He calls for a "r orientation in our intellectual outlook and if that is attainable at all, it surel requires some decades to accomplish. a definitely higher place for the natur sciences—hitherto step-children in th curriculum—any less than one good wa to lift the quality of the training give there in the truly indispensable humani ties and social sciences?

Is softness in our secondary school cu riculum justifiable in the light of th present threat, mode of attack, an strength of our opponent? Call it mere coincidence or rate it vitally meaningfu it is certain that the first nation that ev swept religion completely from its schoo performed immediately thereafter a fe in science education never before a proximated on this planet. Starting 4 years ago with a poor and war-crushe people 70 percent illiterate, it now a nually graduates more than twice as many scientists and engineers as does th United States. That nation now happe to be our dangerous and aggressi enemy. How much longer are we t gamble the fortunes of Western civiliz tion on the proposition that the scientif age is still remote?

OSCAR RIDDL

*Plant City, Florida*


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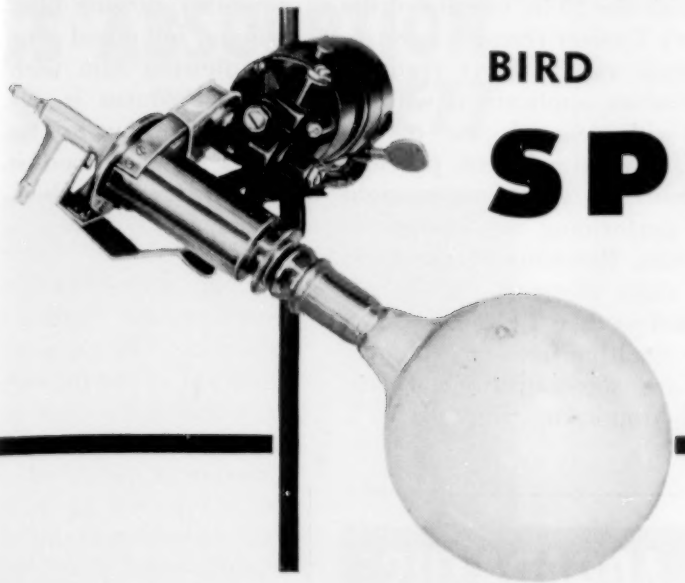

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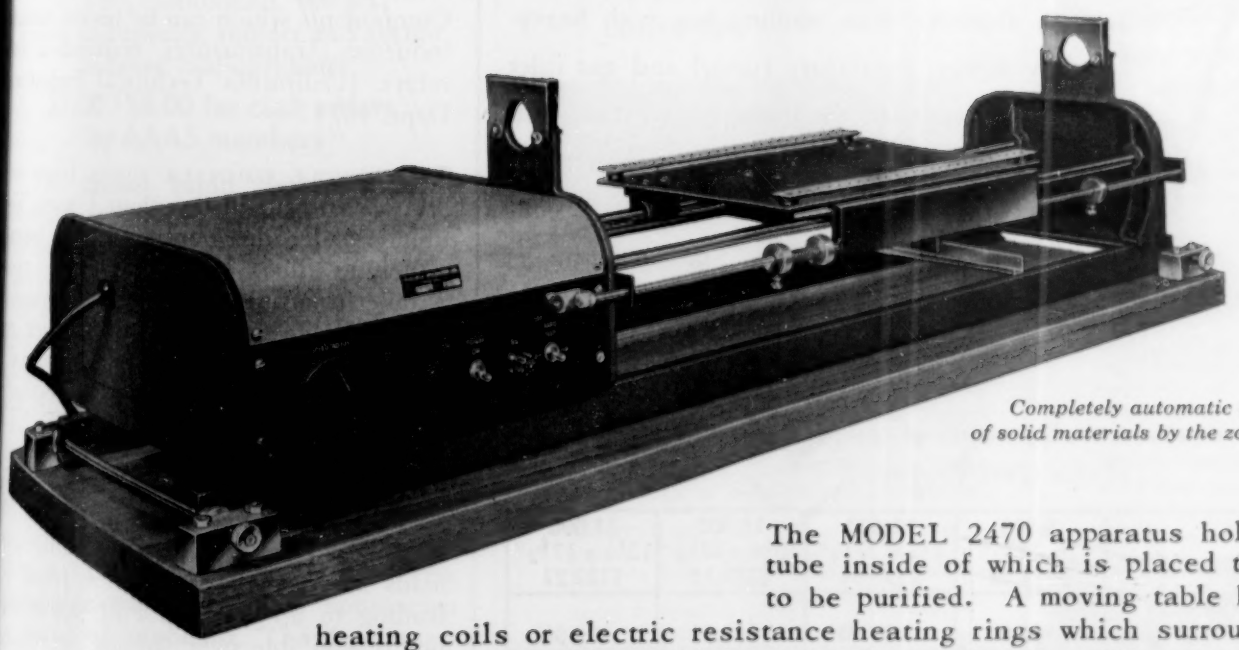

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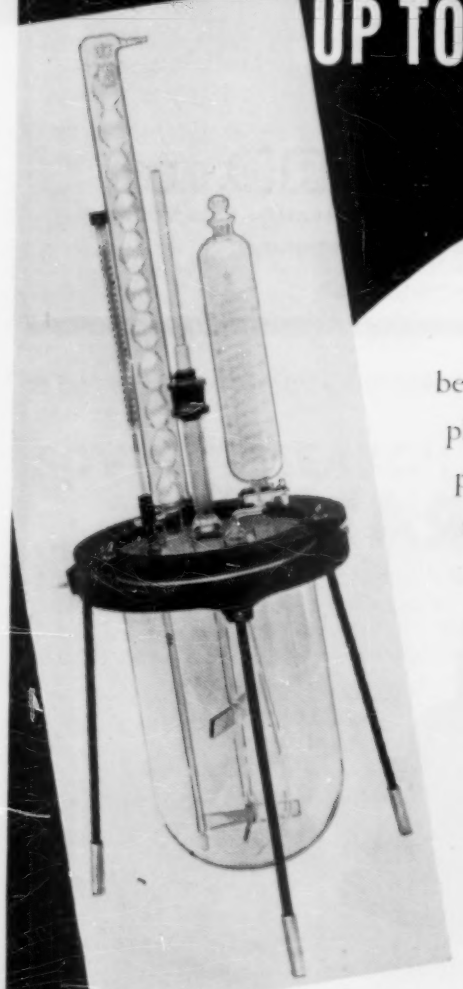

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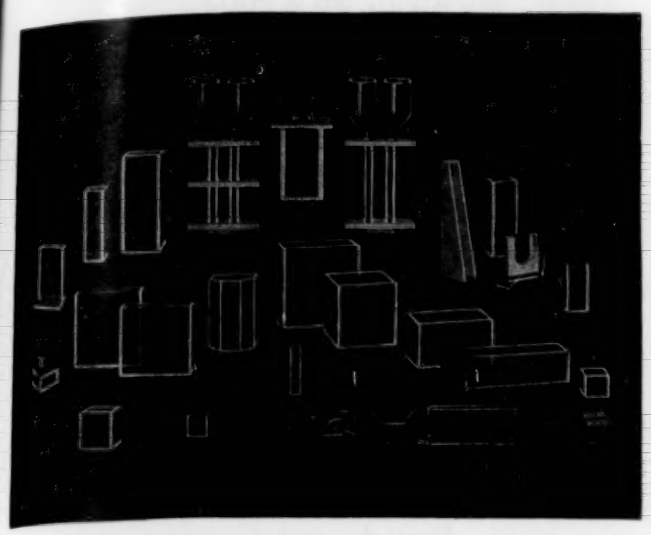

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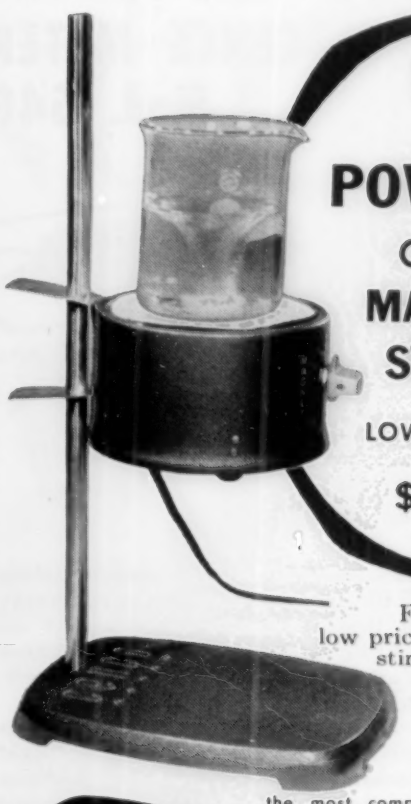

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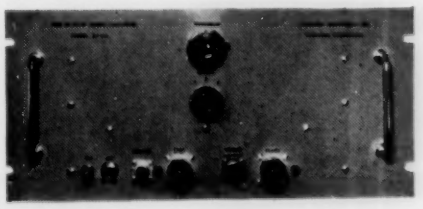

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